10/734,949 EAST

| Ref # | Hits | Search Query | DBs | Default Operator | Plurals | Time Stamp |
|---|---|---|---|---|---|---|
| L1 | 508 | ((514/266.3) or (544/286)).CCLS. | US-PGPUB; USPAT | OR | OFF | 2005/07/12 14:06 |
| L2 | 107 | L1 and (benzyloxy or phenylethyloxy) | US-PGPUB; USPAT | OR | OFF | 2005/07/12 14:06 |

10/ 734,949

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| | | | |
|---|---|---|---|
| NEWS | 1 | | Web Page URLs for STN Seminar Schedule - N. America |
| NEWS | 2 | | "Ask CAS" for self-help around the clock |
| NEWS | 3 | FEB 28 | PATDPAFULL - New display fields provide for legal status data from INPADOC |
| NEWS | 4 | FEB 28 | BABS - Current-awareness alerts (SDIs) available |
| NEWS | 5 | MAR 02 | GBFULL: New full-text patent database on STN |
| NEWS | 6 | MAR 03 | REGISTRY/ZREGISTRY - Sequence annotations enhanced |
| NEWS | 7 | MAR 03 | MEDLINE file segment of TOXCENTER reloaded |
| NEWS | 8 | MAR 22 | KOREAPAT now updated monthly; patent information enhanced |
| NEWS | 9 | MAR 22 | Original IDE display format returns to REGISTRY/ZREGISTRY |
| NEWS | 10 | MAR 22 | PATDPASPC - New patent database available |
| NEWS | 11 | MAR 22 | REGISTRY/ZREGISTRY enhanced with experimental property tags |
| NEWS | 12 | APR 04 | EPFULL enhanced with additional patent information and new fields |
| NEWS | 13 | APR 04 | EMBASE - Database reloaded and enhanced |
| NEWS | 14 | APR 18 | New CAS Information Use Policies available online |
| NEWS | 15 | APR 25 | Patent searching, including current-awareness alerts (SDIs), based on application date in CA/CAplus and USPATFULL/USPAT2 may be affected by a change in filing date for U.S. applications. |
| NEWS | 16 | APR 28 | Improved searching of U.S. Patent Classifications for U.S. patent records in CA/CAplus |
| NEWS | 17 | MAY 23 | GBFULL enhanced with patent drawing images |
| NEWS | 18 | MAY 23 | REGISTRY has been enhanced with source information from CHEMCATS |
| NEWS | 19 | JUN 06 | The Analysis Edition of STN Express with Discover! (Version 8.0 for Windows) now available |
| NEWS | 20 | JUN 13 | RUSSIAPAT: New full-text patent database on STN |
| NEWS | 21 | JUN 13 | FRFULL enhanced with patent drawing images |
| NEWS | 22 | JUN 27 | MARPAT displays enhanced with expanded G-group definitions and text labels |
| NEWS | 23 | JUL 01 | MEDICONF removed from STN |
| NEWS | 24 | JUL 07 | STN Patent Forums to be held in July 2005 |

| | |
|---|---|
| NEWS EXPRESS | JUNE 13 CURRENT WINDOWS VERSION IS V8.0, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 13 JUNE 2005 |
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| NEWS INTER | General Internet Information |
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| NEWS WWW | CAS World Wide Web Site (general information) |

Enter NEWS followed by the item number or name to see news on that

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FILE 'HOME' ENTERED AT 13:31:57 ON 12 JUL 2005

=> file reg

| COST IN U.S. DOLLARS | SINCE FILE ENTRY | TOTAL SESSION |
|---|---|---|
| FULL ESTIMATED COST | 0.21 | 0.21 |

FILE 'REGISTRY' ENTERED AT 13:32:07 ON 12 JUL 2005
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Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 11 JUL 2005 HIGHEST RN 854584-06-8
DICTIONARY FILE UPDATES: 11 JUL 2005 HIGHEST RN 854584-06-8

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TSCA INFORMATION NOW CURRENT THROUGH JANUARY 18, 2005

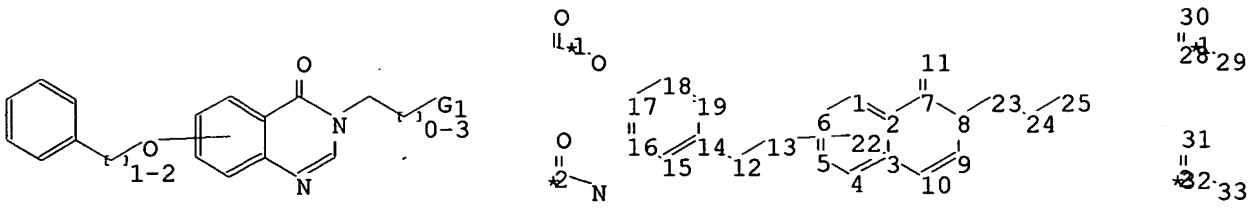
Please note that search-term pricing does apply when conducting SmartSELECT searches.

**********
* *
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added, *
* effective March 20, 2005. A new display format, IDERL, is now *
* available and contains the CA role and document type information. *
* *
**********

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=>
Uploading C:\Program Files\Stnexp\Queries\10734949.str



chain nodes :
11 12 13 23 24 25 28 29 30 31 32 33
ring nodes :
1 2 3 4 5 6 7 8 9 10 14 15 16 17 18 19
chain bonds :
7-11 8-23 12-13 12-14 23-24 24-25 28-29 28-30 31-32 32-33
ring bonds :
1-2 1-6 2-3 2-7 3-4 3-10 4-5 5-6 7-8 8-9 9-10 14-15 14-19 15-16 16-17
17-18 18-19
exact/norm bonds :
2-7 3-10 7-8 7-11 8-9 8-23 9-10 12-13 24-25 28-29 28-30 31-32 32-33
exact bonds :
12-14 23-24
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6 14-15 14-19 15-16 16-17 17-18 18-19
isolated ring systems :
containing 1 : 14 :

G1:O,Ph,CN,N,[*1],[*2]

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:CLASS 12:CLASS 13:CLASS 14:Atom 15:Atom 16:Atom 17:Atom 18:Atom 19:Atom
22:CLASS 23:CLASS 24:CLASS 25:CLASS 28:CLASS 29:CLASS 30:CLASS 31:CLASS
32:CLASS 33:CLASS

L1 STRUCTURE UPLOADED

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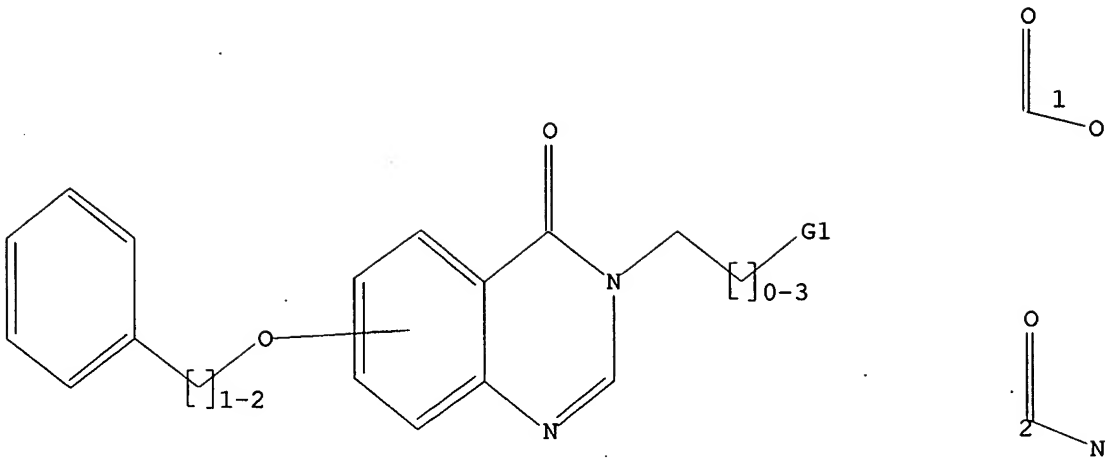
L1 HAS NO ANSWERS
L1 STR




G1 O,Ph,CN,N,[@1],[@2]

Structure attributes must be viewed using STN Express query preparation.

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=> s l1 sample
SAMPLE SEARCH INITIATED 13:32:48 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -   4233 TO ITERATE

 47.2% PROCESSED     2000 ITERATIONS                                 1 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:        80759 TO    88561
PROJECTED ANSWERS:               1 TO      129

L2             1 SEA SSS SAM L1

=> s l1 full
FULL SEARCH INITIATED 13:32:57 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -  87656 TO ITERATE

100.0% PROCESSED    87656 ITERATIONS                                45 ANSWERS
SEARCH TIME: 00.00.04

L3            45 SEA SSS FUL L1

=> file caplus
COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
                                                 ENTRY    SESSION
FULL ESTIMATED COST                              161.76     161.97

FILE 'CAPLUS' ENTERED AT 13:33:05 ON 12 JUL 2005
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FILE COVERS 1907 - 12 Jul 2005 VOL 143 ISS 3
FILE LAST UPDATED: 11 Jul 2005 (20050711/ED)

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This file contains CAS Registry Numbers for easy and accurate substance identification.

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=> s l3
L4           43 L3

=> d his

     (FILE 'HOME' ENTERED AT 13:31:57 ON 12 JUL 2005)

     FILE 'REGISTRY' ENTERED AT 13:32:07 ON 12 JUL 2005
L1               STRUCTURE UPLOADED
L2             1 S L1 SAMPLE
L3            45 S L1 FULL

     FILE 'CAPLUS' ENTERED AT 13:33:05 ON 12 JUL 2005
L4            43 S L3

=> d l4 1- ibib abs hitstr
YOU HAVE REQUESTED DATA FROM 43 ANSWERS - CONTINUE? Y/(N):y
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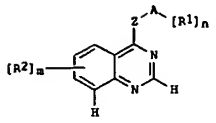
L4 ANSWER 1 OF 43 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2005:141059 CAPLUS
DOCUMENT NUMBER: 142:240453
TITLE: Preparation of quinazolines as inhibitors of VEGF receptor tyrosine kinases
INVENTOR(S): Hennequin, Laurent Francois Andre
PATENT ASSIGNEE(S): Astrazeneca AB, Swed.; Astrazeneca UK Limited
SOURCE: PCT Int. Appl., 124 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2005014582 | A1 | 20050217 | WO 2004-GB3376 | 20040805 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |

PRIORITY APPLN. INFO.: GB 2003-18422 A 20030806
OTHER SOURCE(S): MARPAT 142:240453
GI

L4 ANSWER 1 OF 43 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



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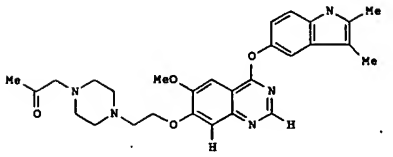


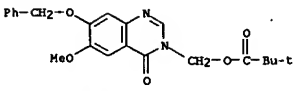
II

AB Title compds. I [wherein A = 8, 9, 10, 12, or 13-membered bicyclic or tricyclic (un)saturated (non)aromatic; Z = O, NH, S; n = 0-5; m = 0-3; R2 = each independently H, OH, halo, CN, NO2, CF3, alkyl, alkoxy, etc.; R1 = each independently H, Me, F; and their salts] were prepared for the manufacture of a medicament for use in the production of an antiangiogenic and/or vascular permeability reducing effect in warm blooded animals. Thus, II was prepared by O-alkylation of 2,3-dimethyl-5-hydroxyindole with 4-chloro-7-(2-chloroethoxy)-6-methoxyquinazoline (preparation given), and amination of the chloride with 1-(acetylmethyl)piperazine. I inhibited gene flt-1 and KDR VEGF receptor tyrosine kinase, FGF, and EGFR receptor with IC50 values < 5 μM in an in vivo test. I inhibited the growth factor--stimulated proliferation of HUVEC cells with IC50 values in the range of 0.001 - 5 μM. II displayed an IC50 = 10.1 μM in an hERG-encoded potassium channel inhibition test. I and their pharmaceutically acceptable salts are useful for treating disease states associated with angiogenesis and/or increased vascular permeability, for e.g. cancer and rheumatoid arthritis.

IT 193002-24-3P, 7-Benzyloxy-6-methoxy-3-[(pivaloyloxy)methyl]-3,4-dihydroquinazolin-4-one
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of quinazolines as inhibitors of VEGF receptor tyrosine kinases and their use for treating angiogenesis and/or increased vascular permeability)

RN 193002-24-3 CAPLUS
CN Propanoic acid, 2,2-dimethyl-, [6-methoxy-4-oxo-7-(phenylmethoxy)-3(4H)-quinazolinyl]methyl ester (9CI) (CA INDEX NAME)

L4 ANSWER 1 OF 43 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 43 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:1059177 CAPLUS
DOCUMENT NUMBER: 142:38269
TITLE: Preparation of (3-((quinazolin-4-yl)amino)-1H-pyrazol-1-yl)acetamide derivatives and related compounds as aurora kinase inhibitors for the treatment of proliferative diseases such as cancer
INVENTOR(S): Mortlock, Andrew Austen; Heron, Nicola Murdoch; Jung, Frederic Henri; Pasquet, Georges Rene
PATENT ASSIGNEE(S): Astrazeneca AB, Swed.; Astrazeneca UK Limited
SOURCE: PCT Int. Appl., 66 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2004105764 | A1 | 20041209 | WO 2004-GB2281 | 20040527 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |

PRIORITY APPLN. INFO.: EP 2003-291314 A 20030602
OTHER SOURCE(S): MARPAT 142:38269
GI

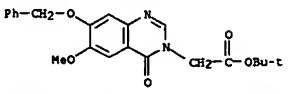
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Quinazoline derivs. I [X = O, NR6; R1-R4 = independently H, halo, X1R7; R5 = optionally substituted aryl, heteroaryl; R6 = H, C1-4 alkyl; X1 = bond, O, NH, N(C1-6 alkyl); R7 = H, optionally substituted heterocyclyl, C1-6 alkyl, C2-6 alkenyl, C2-6 alkynyl, C3-6 cycloalkyl, C3-6 cycloalkenyl] for use in the treatment of proliferative diseases such as cancer and in the preparation of medicaments for use in the treatment of proliferative diseases, and to processes for their preparation, as well as pharmaceutical compns. containing, them as active ingredient. Thus, coupling of chloroquinazoline II (preparation given) with aminopyrazole III (preparation given), followed by substitution with D-prolinol gave title compound IV.

IT 557771-41-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of (quinazolinylamino)pyrazolylacetamide derivs. as aurora kinase inhibitors and anticancer agents)

RN 557771-41-2 CAPLUS
CN 3(4H)-Quinazolineacetic acid, 6-methoxy-4-oxo-7-(phenylmethoxy)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

L4 ANSWER 2 OF 43 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 43 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:995977 CAPLUS
DOCUMENT NUMBER: 141:420417
TITLE: Therapeutic agents comprising an anti-angiogenic agent in combination with an Src inhibitor for use in normotensive treatment of angiogenesis
INVENTOR(S): Curven, Jon Owen; Wedge, Stephen Robert
PATENT ASSIGNEE(S): Astrazeneca AB, Swed.; Astrazeneca UK Limited
SOURCE: PCT Int. Appl., 111 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2004098604 | A1 | 20041118 | WO 2004-GB1939 | 20040504 |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: GB 2003-10401 A 20030507
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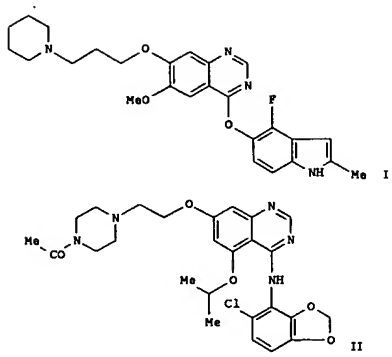
L4 ANSWER 3 OF 43 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



I



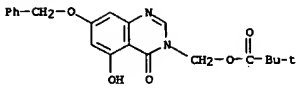
II

AB The invention relates to the use of an anti-angiogenic agent, such as I (preparation given), in combination with an inhibitor of the Src family of non-receptor tyrosine kinases, such as the II (prepns. according to a previous patent given), in the manufacture of a medicament for use in the substantially normotensive treatment in a warm-blooded mammal such as a human being of a disease state associated with angiogenesis. The invention provides for the Src kinase inhibitor to be administered in an amount effective to counteract substantially the hypertension induced by the anti-angiogenic agent. Thus, 7-(2-chloroethoxy)-4-(6-chloro-2,3-methylenedioxyanilino)-5-isopropoxyquinazoline was coupled with 1-acetylpiperazine using KI in DMA to give I. The diastolic blood pressure profile of rats over a 24 h period after administration of a combination of 1.5 mg/kg of I and 25 mg/kg of II demonstrated that the contrasting blood pressure effects of the antiangiogenic agent and the Src kinase inhibitor were substantially counterbalanced.

IT 379229-61-5, 7-Benzyloxy-5-hydroxy-3-[(pivaloyloxy)methyl]-3,4-dihydroquinazolin-4-one
RL: RCT (Reactant); RACT (Reactant or reagent)
(therapeutic agents comprising an anti-angiogenic agent in combination with an Src inhibitor for use in normotensive treatment of angiogenesis)

RN 379229-61-5 CAPLUS
CN Propanoic acid, 2,2-dimethyl-, [5-hydroxy-4-oxo-7-(phenylmethoxy)-3(4H)-quinazolinyl]methyl ester (9CI) (CA INDEX NAME)

L4 ANSWER 3 OF 43 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 43 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:965069 CAPLUS
DOCUMENT NUMBER: 141:410946
TITLE: Preparation of (anilino)quinazoline derivatives as erbB tyrosine kinase inhibitors for the treatment of cancer
INVENTOR(S): Hennequin, Laurent Francois Andre; Plowright, Alleyn
PATENT ASSIGNEE(S): AstraZeneca AB, Swed.; AstraZeneca UK Limited
SOURCE: PCT Int. Appl., 131 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2004096226 | A1 | 20041111 | WO 2004-GB1799 | 20040427 |

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RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: GB 2003-9850 A 20030430
OTHER SOURCE(S): MARPAT 141:410946
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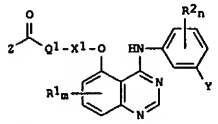

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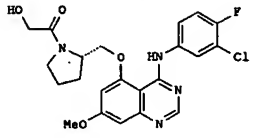


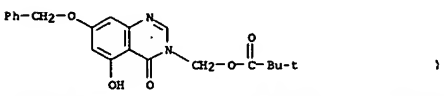
II

L4 ANSWER 4 OF 43 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

AB Title compds. represented by the formula I [wherein R1 = independently HO, alkoxy, alkenyloxy, alkynyloxy, etc.; R2 = independently halo, cyano, nitro, carbamoyl, etc.; X1 = (alkyl)methylene; Q1 = pyrrolidinyl; Z = (halo)alkyl, alkoxyalkyl, (alkyl)aminoalkyl, etc.; m = 0-2; Y = halo, cyano, CF3, alkyl, etc.; n = 0-4; and pharmaceutically acceptable salts thereof] were prepared as erbB tyrosine kinase inhibitors, particularly EGFR tyrosine kinase inhibitors. For example, II was given in a multi-step synthesis starting from N-(3-chloro-4-fluorophenyl)-7-methoxy-5-((2S)-pyrrolidin-2-ylmethoxy)quinazolin-4-amine. Selected I were tested for inhibition of EGFR and erbB2 tyrosine kinase protein phosphorylation, and EGFR driven KB cell proliferation. Thus, I and their pharmaceutical compns. are useful for the treatment of erbB tyrosine kinase mediated diseases such as cancer (no data).

IT 379229-61-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of 4-anilinoquinazoline derivs. as erbB tyrosine kinase inhibitors for treatment of cancer)

RN 379229-61-5 CAPLUS
CN Propanoic acid, 2,2-dimethyl-, [5-hydroxy-4-oxo-7-(phenylmethoxy)-3(4H)-quinazolinyl]methyl ester (9CI) (CA INDEX NAME)



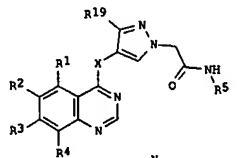
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 5 OF 43 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:927198 CAPLUS
DOCUMENT NUMBER: 141:395569
TITLE: Quinazoline derivatives as aurora kinase inhibitors, process for their preparations, pharmaceutical compositions and uses in the treatment of proliferative diseases
INVENTOR(S): Heron, Nicola Murdoch; Pasquet, Georges Rene; Mortlock, Andrew Austen; Jung, Frederic Henri
PATENT ASSIGNEE(S): Astrazeneca AB, Swed.; Astrazeneca UK Limited
SOURCE: PCT Int. Appl., 300 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

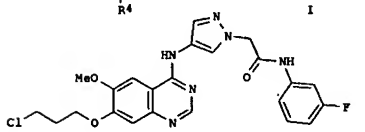
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2004094410 | A1 | 20041104 | WO 2004-GB1614 | 20040414 |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: EP 2003-290951 A 20030416
OTHER SOURCE(S): MARPAT 141:395569
GI



I



II

AB Quinazoline derivs. of formula I [wherein X = O, NH or N(alkyl); R1-R4 =

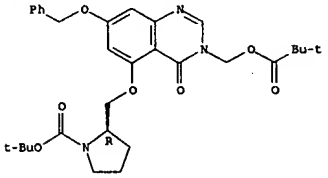
L4 ANSWER 5 OF 43 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

H, halo or alkoxy; R2 = nitro, cyano, OPO3H2; R3 = phosphonooxyalkoxy; R5 = (un)substituted (hetero)aryl; R19 = H, alkyl, acyl, amide, ester, etc.; and salts, esters or prodrugs thereof] were prepd. as aurora kinase inhibitors. Thus, II was synthesized in 95% yield by condensation of the corresponding 4-chloroquinazoline deriv. (prepn. given) with 4-aminopyrazole deriv. (prepn. given). Compds. I generally showed 50% inhibition activity at the concns. of 1-1000 nM against both aurora-A and aurora-B kinases, and were active in the in vitro cell proliferation assay and in the in vitro cell cycle anal. assay at the concns. of 1 nM to 100 μM and 1 nM to 10 μM, resp. Also disclosed are processes for the prepns. of I, pharmaceutical compns. comprising I and uses of I for the treatment of proliferative diseases such as cancer.

IT 786684-90-0P, tert-Butyl (2R)-2-[[[7-(benzyloxy)-3-[[(2,2-dimethylpropanoyl)oxy]methyl]-4-oxo-3,4-dihydroquinazolin-5-yl]oxy]methyl]pyrrolidine-1-carboxylate
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of quinazoline derivs. as aurora kinase inhibitors)

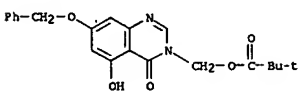
RN 786684-90-0 CAPLUS
CN 1-Pyrrolidinecarboxylic acid, 2-[[[3-[(2,2-dimethyl-1-oxopropoxy)methyl]-3,4-dihydro-4-oxo-7-(phenylmethoxy)-5-quinazolinyl]oxy]methyl]-, 1,1-dimethylethyl ester, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 379229-61-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(reactant; preparation of quinazoline derivs. as aurora kinase inhibitors)

RN 379229-61-5 CAPLUS
CN Propanoic acid, 2,2-dimethyl-, [5-hydroxy-4-oxo-7-(phenylmethoxy)-3(4H)-quinazolinyl]methyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 5 OF 43 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

L4 ANSWER 6 OF 43 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:857372 CAPLUS
DOCUMENT NUMBER: 141:350196
TITLE: Preparation of quinazoline derivatives as selective Src kinase inhibitors
INVENTOR(S): Curwen, Jon Owen
PATENT ASSIGNEE(S): Astrazeneca Ab, Swed.; Astrazeneca UK Limited
SOURCE: PCT Int. Appl., 58 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2004087120 | A2 | 20041014 | WO 2004-GB1286 | 20040323 |
| WO 2004087120 | A3 | 20050127 | | |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

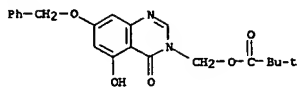
PRIORITY APPLN. INFO.: GB 2003-7333 A 20030329

AB The invention relates to the use of quinazoline derivative as a Src kinase inhibitor in the production of a medicament for use in the prophylaxis or treatment of hypertension. More particularly, the invention concerns the anti-hypertensive use of a selective Src kinase inhibitor that possess less potent VEGF receptor tyrosine kinase inhibitory properties. The invention also relates to a combination product comprising a Src kinase inhibitor and one or more further anti-hypertensive agents and to the use of Src kinase inhibitors as primary regulators of cardiovascular disease and in the prevention of stroke. For example, 7-[2-(4-acetylpiperazin-1-yl)ethoxy]-4-(5-chloro-2,3-methylenedioxypyrid-4-ylamino)-5-isopropoxyquinazoline administered to rats at 25 mg/kg p.o. on day 1 showed hypotensive effect of 25 mmHg on day 2.

IT 379229-61-5, 7-Benzyloxy-5-hydroxy-3-pivaloyloxymethyl-3,4-dihydroquinazolin-4-one
RL: RCT (Reactant); RACT (Reactant or reagent)
(reactant; preparation of quinazoline derivs. as selective Src kinase inhibitors and regulators of cardiovascular disease for prophylaxis or treatment of hypertension or for prevention of stroke)

RN 379229-61-5 CAPLUS
CN Propanoic acid, 2,2-dimethyl-, [5-hydroxy-4-oxo-7-(phenylmethoxy)-3(4H)-quinazolinyl]methyl ester (9CI) (CA INDEX NAME)

L4 ANSWER 6 OF 43 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)




L4 ANSWER 7 OF 43 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:701950 CAPLUS
DOCUMENT NUMBER: 141:200165
TITLE: ZD6474 combination with 5-FU and/or CPT-11 for the treatment of cancer
INVENTOR(S): Wedge, Stephen Robert; Ryan, Anderson Joseph
PATENT ASSIGNEE(S): Astrazeneca AB, Swed.; Astrazeneca UK Limited
SOURCE: PCT Int. Appl., 43 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2004071397 | A2 | 20040826 | WO 2004-GB550 | 20040211 |
| WO 2004071397 | A3 | 20041014 | | |

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RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

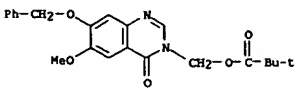
PRIORITY APPLN. INFO.:
GB 2003-3289 A 20030213
GB 2003-14100 A 20030618
GB 2003-16184 A 20030710
GB 2003-18311 A 20030805

AB The invention relates to a method for the production of an antiangiogenic and/or vascular permeability-reducing effect in a warm-blooded animal, e.g. a human, which is optionally being treated with ionizing radiation, particularly a method for the treatment of a cancer, particularly a cancer involving a solid tumor, which comprises one of: the administration of ZD6474 in combination with 5-FU; the administration of ZD6474 in combination with CPT-11; and the administration of ZD6474 in combination with 5-FU and CPT-11; to a pharmaceutical composition comprising one of: ZD6474 and 5-FU; ZD6474 and CPT-11; and ZD6474 and 5-FU and CPT-11; to a combination product comprising one of: ZD6474 and 5-FU; ZD6474 and CPT-11; and ZD6474 and 5-FU and CPT-11, for use in a method of treatment of a human or animal body by therapy; to a kit comprising one of: ZD6474 and 5-FU; ZD6474 and CPT-11; and ZD6474 and 5-FU and CPT-11; to the use of one of: ZD6474 and 5-FU; ZD6474 and CPT-11; and ZD6474 and 5-FU and CPT-11, in the manufacture of a medicament for use in the production of an antiangiogenic and/or vascular permeability reducing effect in a warm-blooded animal, e.g. a human, which is optionally being treated with ionizing radiation. Preparation of ZD6474 is described.

IT 193002-24-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(ZD6474 combination with 5-FU and/or CPT-11 for treatment of cancer)

RN 193002-24-3 CAPLUS
CN Propanoic acid, 2,2-dimethyl-, [6-methoxy-4-oxo-7-(phenylmethoxy)-3(4H)-quinazolinyl]methyl ester (9CI) (CA INDEX NAME)

L4 ANSWER 7 OF 43 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



L4 ANSWER 8 OF 43 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:566625 CAPLUS
DOCUMENT NUMBER: 141:123758
TITLE: Preparation of phosphonooxy quinazoline derivatives as therapeutic agents
INVENTOR(S): Mortlock, Andrew Austen
PATENT ASSIGNEE(S): Astrazeneca Ab, Swed.; Astrazeneca Uk Limited
SOURCE: PCT Int. Appl., 97 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2004058782 | A1 | 20040715 | WO 2003-GB5640 | 20031222 |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: EP 2002-293240 A 20021224
OTHER SOURCE(S): MARPAT 141:123758
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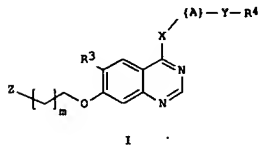


I

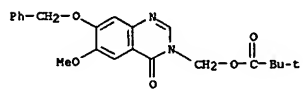
AB Preparation of phosphonooxy quinazoline derivs. I (A = 6-membered heteroaryl containing nitrogen atom and optionally containing one or two further nitrogen atoms; X = O, S, S(O), S(O)2, organoamino; m = 0-4; Y = O, carbonylamido, etc.; Z = organoamino, phosphonooxy, C3-6 (un)substituted phosphonooxy cycloalkyl, etc.; R3 = H, halo, cyano, nitro, C1-6 alkoxy, C1-6 alkyl, carbonylamido, sulfonylamido, organoamino, etc.; R4 = H, C1-4 alkyl, heteroaryl, heteroaryl C1-4 alkyl, aryl, aryl C1-4 alkyl, halo Me Et, cyclopropyl, ethynyl substituted alkyl, etc.), compns. containing them, processes for their preparation and their use in therapy, is described. Thus, reaction of N-(6-[(3-chlorobenzyl)oxy]pyridin-3-yl)-7-(3-chloropropoxy)-6-

L4 ANSWER 8 OF 43 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

methoxyquinazolin-4-amine (prepn. given) with 3-amino-3-methylbutanol in di-Me acetamide in the presence of KI gave 75% 3-[(3-{[4-{[6-[(3-chlorobenzyl)oxy]pyridin-3-yl}amino)-6-methoxyquinazolin-7-yl]oxy}propyl)amino]-3-methylbutan-1-ol which on treatment with di-tert-butyl-N,N-diethylphosphoramidite, oxidn. with H2O2, and hydrolysis of the formed phosphate ester gave title compd., 3-[(3-{[4-{[6-[(3-chlorobenzyl)oxy]pyridin-3-yl}amino]-6-methoxyquinazolin-7-yl]oxy}propyl)amino]-3-methylbutyl dihydrogen phosphate.

IT 193002-24-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of phosphonooxy quinazoline derivs. as therapeutic agents)

RN 193002-24-3 CAPLUS
CN Propanoic acid, 2,2-dimethyl-, [6-methoxy-4-oxo-7-(phenylmethoxy)-3(4H)-quinazolinyl]methyl ester (9CI) (CA INDEX NAME)



L4 ANSWER 9 OF 43 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:534181 CAPLUS
DOCUMENT NUMBER: 141:89098
TITLE: Preparation of 3H-quinazolin-4-one derivatives as selective monoamine oxidase B inhibitors
INVENTOR(S): Rodriguez, Sarmiento Rosa Maria; Thomas, Andrew William; Wyler, Rene
PATENT ASSIGNEE(S): F. Hoffmann-La Roche Ag, Switz.
SOURCE: PCT Int. Appl., 29 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2004054985 | A1 | 20040701 | WO 2003-EP13888 | 20031208 |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW
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US 2004142951 A1 20040722 US 2003-734949 20031213
PRIORITY APPLN. INFO.: EP 2002-27700 A 20021213
OTHER SOURCE(S): MARPAT 141:89098
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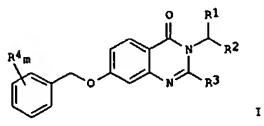
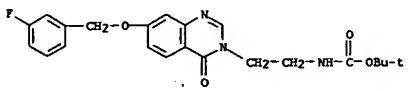


I

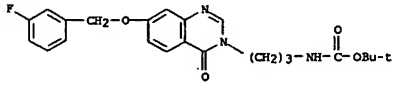
AB Title compds. I (R1 = aminocarbonylalkyl, carboxyalkyl, alkoxycarbonylalkyl, cyanoalkyl, hydroxyalkyl, alkoxyalkyl, Ph, etc.; R2 = H, halo, alkyl; R3 = H, alkyl, cycloalkyl, benzyl; R4 = halo, fluoroalkyl, cyano, alkoxy, fluoroalkoxy; m = 1, 2, 3) and their pharmaceutically acceptable salts are prepared I are useful for the treatment of Alzheimer's disease and senile dementia. Formulations containing I were given.

IT 713511-13-9P, [2-[7-(3-Fluorobenzyloxy)-4-oxo-4H-quinazolin-3-yl]ethyl]carbamic acid tert-butyl ester 713511-14-9P, [3-[7-(3-Fluorobenzyloxy)-4-oxo-4H-quinazolin-3-yl]propyl]carbamic acid tert-butyl ester 713511-17-2P, [2-[7-(4-Fluorobenzyloxy)-4-oxo-4H-quinazolin-3-yl]ethyl]carbamic acid tert-butyl ester 713511-23-0P, [2-[7-(3-Fluorobenzyloxy)-2-methyl-4-oxo-4H-quinazolin-3-yl]ethyl]carbamic acid tert-butyl ester
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of quinazolinone derivs. as selective monoamine oxidase B

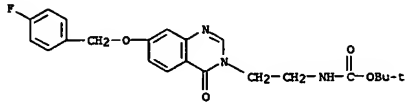
L4 ANSWER 9 OF 43 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
inhibitors)
RN 713511-13-8 CAPLUS
CN Carbamic acid, [2-[7-[(3-fluorophenyl)methoxy]-4-oxo-3(4H)-quinazolinyl]ethyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



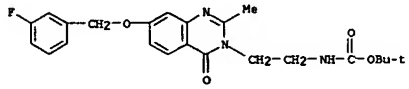
RN 713511-14-9 CAPLUS
CN Carbamic acid, [3-[7-[(3-fluorophenyl)methoxy]-4-oxo-3(4H)-quinazolinyl]propyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



RN 713511-17-2 CAPLUS
CN Carbamic acid, [2-[7-[(4-fluorophenyl)methoxy]-4-oxo-3(4H)-quinazolinyl]ethyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

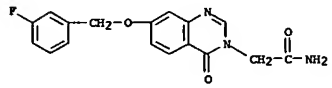


RN 713511-23-0 CAPLUS
CN Carbamic acid, [2-[7-[(3-fluorophenyl)methoxy]-2-methyl-4-oxo-3(4H)-quinazolinyl]ethyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

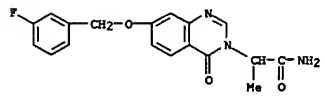


IT 713511-06-9P, 2-[7-(3-Fluorobenzyloxy)-2-isopropyl-4-oxo-4H-quinazolin-3-yl]acetamide

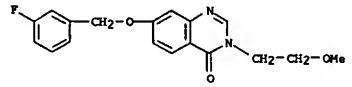
L4 ANSWER 9 OF 43 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
RN 713510-85-1 CAPLUS
CN 3(4H)-Quinazolineacetamide, 7-[(3-fluorophenyl)methoxy]-4-oxo- (9CI) (CA INDEX NAME)



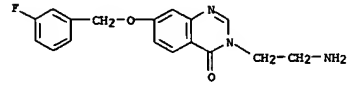
RN 713510-86-2 CAPLUS
CN 3(4H)-Quinazolineacetamide, 7-[(3-fluorophenyl)methoxy]-α-methyl-4-oxo- (9CI) (CA INDEX NAME)



RN 713510-87-3 CAPLUS
CN 4(3H)-Quinazolinone, 7-[(3-fluorophenyl)methoxy]-3-(2-methoxyethyl)- (9CI) (CA INDEX NAME)



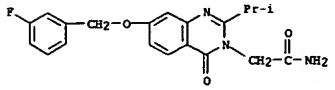
RN 713510-88-4 CAPLUS
CN 4(3H)-Quinazolinone, 3-(2-aminoethyl)-7-[(3-fluorophenyl)methoxy]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

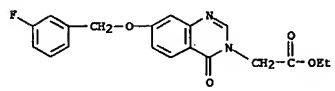
RN 713510-89-5 CAPLUS
CN 3(4H)-Quinazolineacetic acid, 7-[(3-fluorophenyl)methoxy]-4-oxo-, ethyl ester (9CI) (CA INDEX NAME)

L4 ANSWER 9 OF 43 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
RL: RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of quinazolinone derivs. as selective monoamine oxidase B inhibitors)
RN 713511-06-9 CAPLUS
CN 3(4H)-Quinazolineacetamide, 7-[(3-fluorophenyl)methoxy]-2-(1-methylethyl)-4-oxo- (9CI) (CA INDEX NAME)

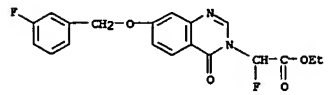


IT 713510-85-1P, 2-[7-(3-Fluorobenzyloxy)-4-oxo-4H-quinazolin-3-yl]acetamide 713510-86-2P, 2-[7-(3-Fluorobenzyloxy)-4-oxo-4H-quinazolin-3-yl]propionamide 713510-87-3P, 7-(3-Fluorobenzyloxy)-3-(2-methoxyethyl)-3H-quinazolin-4-one 713510-88-4P, 3-(2-Aminoethyl)-7-(3-fluorobenzyloxy)-3H-quinazolin-4-one dihydrochloride 713510-89-5P, [7-(3-Fluorobenzyloxy)-4-oxo-4H-quinazolin-3-yl]acetic acid ethyl ester 713510-90-8P, Fluoro-[7-(3-fluorobenzyloxy)-4-oxo-4H-quinazolin-3-yl]acetic acid ethyl ester 713510-91-9P, 2-[7-(3-Fluorobenzyloxy)-4-oxo-4H-quinazolin-3-yl]propionic acid ethyl ester 713510-92-0P, [7-(3-Fluorobenzyloxy)-4-oxo-4H-quinazolin-3-yl]acetic acid tert-butyl ester 713510-93-1P, 2-[7-(3-Fluorobenzyloxy)-4-oxo-4H-quinazolin-3-yl]propionic acid tert-butyl ester 713510-94-2P, 3-(3-Aminopropyl)-7-(3-fluorobenzyloxy)-3H-quinazolin-4-one dihydrochloride 713510-96-4P, 2-[7-(4-Fluorobenzyloxy)-4-oxo-4H-quinazolin-3-yl]acetamide 713510-97-5P, 2-[7-(4-Fluorobenzyloxy)-4-oxo-4H-quinazolin-3-yl]propionamide 713510-98-6P, [7-(4-Fluorobenzyloxy)-4-oxo-4H-quinazolin-3-yl]acetic acid ethyl ester 713510-99-7P, 2-[7-(4-Fluorobenzyloxy)-4-oxo-4H-quinazolin-3-yl]propionic acid ethyl ester 713511-00-3P, 7-(4-Fluorobenzyloxy)-3-(2-methoxyethyl)-3H-quinazolin-4-one 713511-01-4P, 3-(2-Aminoethyl)-7-(4-fluorobenzyloxy)-3H-quinazolin-4-one hydrochloride 713511-02-5P, 3-[7-(4-Fluorobenzyloxy)-4-oxo-4H-quinazolin-3-yl]propionamide 713511-03-6P, 2-[7-(3-Fluorobenzyloxy)-2-methyl-4-oxo-4H-quinazolin-3-yl]acetamide 713511-04-7P, 7-(3-Fluorobenzyloxy)-3-(2-methoxyethyl)-2-methyl-3H-quinazolin-4-one 713511-05-8P 713511-07-0P, [7-(3-Fluorobenzyloxy)-2-isopropyl-4-oxo-4H-quinazolin-3-yl]acetonitrile 713511-08-1P, 2-[2-Cyclopropyl-7-(3-fluorobenzyloxy)-4-oxo-4H-quinazolin-3-yl]acetamide 713511-09-2P, 2-Cyclopropyl-7-(3-fluorobenzyloxy)-3-(2-methoxyethyl)-3H-quinazolin-4-one 713511-10-5P, [2-Cyclopropyl-7-(3-fluorobenzyloxy)-4-oxo-4H-quinazolin-3-yl]acetic acid methyl ester 713511-11-6P, 2-[2-Benzyl-7-(3-fluorobenzyloxy)-4-oxo-4H-quinazolin-3-yl]acetamide
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of quinazolinone derivs. as selective monoamine oxidase B inhibitors)

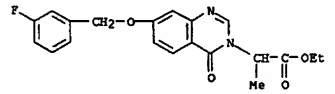
L4 ANSWER 9 OF 43 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



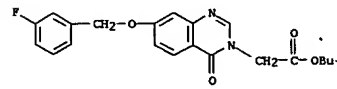
RN 713510-90-8 CAPLUS
CN 3(4H)-Quinazolineacetic acid, α-fluoro-7-[(3-fluorophenyl)methoxy]-4-oxo-, ethyl ester (9CI) (CA INDEX NAME)



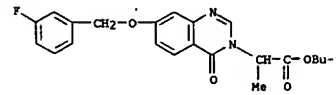
RN 713510-91-9 CAPLUS
CN 3(4H)-Quinazolineacetic acid, 7-[(3-fluorophenyl)methoxy]-α-methyl-4-oxo-, ethyl ester (9CI) (CA INDEX NAME)



RN 713510-92-0 CAPLUS
CN 3(4H)-Quinazolineacetic acid, 7-[(3-fluorophenyl)methoxy]-4-oxo-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

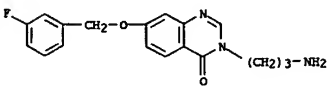


RN 713510-93-1 CAPLUS
CN 3(4H)-Quinazolineacetic acid, 7-[(3-fluorophenyl)methoxy]-α-methyl-4-oxo-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



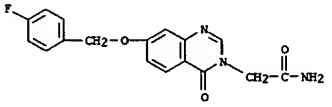
L4 ANSWER 9 OF 43 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

RN 713510-94-2 CAPLUS
CN 4(3H)-Quinazolinone, 3-(3-aminopropyl)-7-[(3-fluorophenyl)methoxy]-, dihydrochloride (9CI) (CA INDEX NAME)

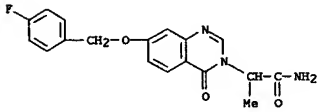


●2 HCl

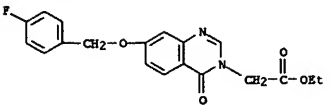
RN 713510-96-4 CAPLUS
CN 3(4H)-Quinazolineacetamide, 7-[(4-fluorophenyl)methoxy]-4-oxo- (9CI) (CA INDEX NAME)



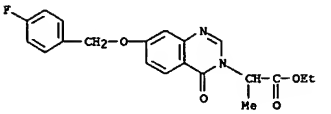
RN 713510-97-5 CAPLUS
CN 3(4H)-Quinazolineacetamide, 7-[(4-fluorophenyl)methoxy]-α-methyl-4-oxo- (9CI) (CA INDEX NAME)



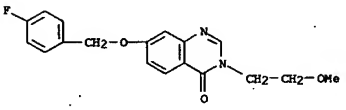
RN 713510-98-6 CAPLUS
CN 3(4H)-Quinazolineacetic acid, 7-[(4-fluorophenyl)methoxy]-4-oxo-, ethyl ester (9CI) (CA INDEX NAME)



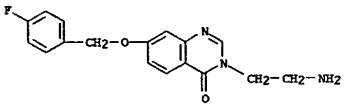
RN 713510-99-7 CAPLUS
CN 3(4H)-Quinazolineacetic acid, 7-[(4-fluorophenyl)methoxy]-α-methyl-4-oxo-, ethyl ester (9CI) (CA INDEX NAME)



RN 713511-00-3 CAPLUS
CN 4(3H)-Quinazolinone, 7-[(4-fluorophenyl)methoxy]-3-(2-methoxyethyl)- (9CI) (CA INDEX NAME)



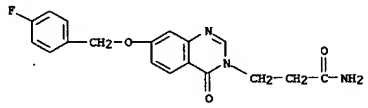
RN 713511-01-4 CAPLUS
CN 4(3H)-Quinazolinone, 3-(2-aminoethyl)-7-[(4-fluorophenyl)methoxy]-, monohydrochloride (9CI) (CA INDEX NAME)



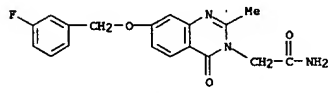
● HCl

L4 ANSWER 9 OF 43 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

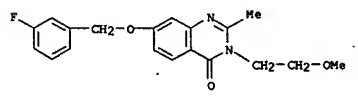
RN 713511-02-5 CAPLUS
CN 3(4H)-Quinazolinepropanamide, 7-[(4-fluorophenyl)methoxy]-4-oxo- (9CI) (CA INDEX NAME)



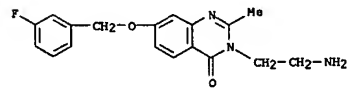
RN 713511-03-6 CAPLUS
CN 3(4H)-Quinazolineacetamide, 7-[(3-fluorophenyl)methoxy]-2-methyl-4-oxo- (9CI) (CA INDEX NAME)



RN 713511-04-7 CAPLUS
CN 4(3H)-Quinazolinone, 7-[(3-fluorophenyl)methoxy]-3-(2-methoxyethyl)-2-methyl- (9CI) (CA INDEX NAME)



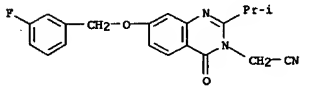
RN 713511-05-8 CAPLUS
CN 4(3H)-Quinazolinone, 3-(2-aminoethyl)-7-[(3-fluorophenyl)methoxy]-2-methyl-, monohydrochloride (9CI) (CA INDEX NAME)



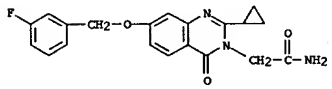
● HCl

RN 713511-07-0 CAPLUS
CN 3(4H)-Quinazolineacetonitrile, 7-[(3-fluorophenyl)methoxy]-2-(1-

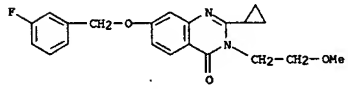
L4 ANSWER 9 OF 43 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
methylethyl)-4-oxo- (9CI) (CA INDEX NAME)



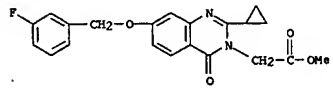
RN 713511-08-1 CAPLUS
CN 3(4H)-Quinazolineacetamide, 2-cyclopropyl-7-[(3-fluorophenyl)methoxy]-4-oxo- (9CI) (CA INDEX NAME)



RN 713511-09-2 CAPLUS
CN 4(3H)-Quinazolinone, 2-cyclopropyl-7-[(3-fluorophenyl)methoxy]-3-(2-methoxyethyl)- (9CI) (CA INDEX NAME)

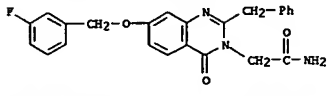


RN 713511-10-5 CAPLUS
CN 3(4H)-Quinazolineacetic acid, 2-cyclopropyl-7-[(3-fluorophenyl)methoxy]-4-oxo-, methyl ester (9CI) (CA INDEX NAME)



RN 713511-11-6 CAPLUS
CN 3(4H)-Quinazolineacetamide, 7-[(3-fluorophenyl)methoxy]-4-oxo-2-(phenylmethyl)- (9CI) (CA INDEX NAME)

L4 ANSWER 9 OF 43 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

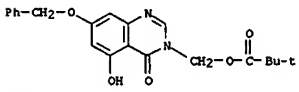
L4 ANSWER 10 OF 43 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

tumor cells derived from the COLO 357 human pancreatic cancer cell line and treated with gemcitabine, the Src inhibitor, 4-(2-chloro-5-methoxyanilino)-6-methoxy-7-(N-methylpiperidin-4-ylmethoxy)quinazoline, or a combination of the two. Evaluation for tumor growth and incidence of liver metastases showed that, compared with the wt. of control tumors, tumor growth in animals treated with the combination was much reduced (1359 mg and 124 mg, resp.) to a level well below that achievable on the dosing of either gemcitabine or the Src inhibitor alone. In addn., there was no liver metastasis in the animals treated with the combination, whereas liver metastasis was present in 1/5 of the animals treated with gemcitabine alone.

IT **379229-61-5**, 7-Benzyloxy-5-hydroxy-3-[(pivaloyloxy)methyl]-3,4-dihydroquinazolin-4-one
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of quinazoline-containing Src inhibitors for use in synergistic
combination with gemcitabine for treatment and prophylaxis of pancreatic cancer)

RN 379229-61-5 CAPLUS

CN Propanoic acid, 2,2-dimethyl-, [5-hydroxy-4-oxo-7-(phenylmethoxy)-3(4H)-quinazolinyl]methyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

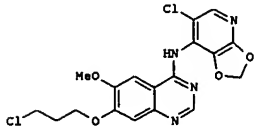
L4 ANSWER 10 OF 43 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:430753 CAPLUS
DOCUMENT NUMBER: 141:1220
TITLE: Preparation of quinazolines as Src family non-receptor tyrosine kinase inhibitors for use in combination therapy with gemcitabine for treatment and prophylaxis of pancreatic cancer
INVENTOR(S): Barge, Alan
PATENT ASSIGNEE(S): Astrazeneca AB, Swed.; Astrazeneca UK Limited
SOURCE: PCT Int. Appl., 75 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2004043472 | A1 | 20040527 | WO 2003-GB4787 | 20031107 |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: GB 2002-26434 A 20021113
GI



I

AB The invention concerns a combination comprising an inhibitor of Src kinase and the cytotoxic agent, gemcitabine, a pharmaceutical composition comprising
such a combination, and its use in the treatment or prophylaxis of cancer, particularly of pancreatic cancer. Examples include prepns. for anilino- and (pyridylamino)quinazoline Src inhibitors (no Markush structure given) and bioassays demonstrating the synergistic effect of treating pancreatic cancer with a quinazoline Src inhibitor in combination with gemcitabine. For instance, 4-amino-5-chloro-2,3-methylenedioxypyridine was coupled with 4-chloro-7-(3-chloropropoxy)-6-methoxyquinazoline (preparation of reactants given) in the presence of sodium hexamethyldisilazane in THF to afford the (pyridylamino)quinazoline I. Nude mice were injected with pancreatic

L4 ANSWER 11 OF 43 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:414727 CAPLUS
DOCUMENT NUMBER: 140:423698
TITLE: Preparation of quinazoline derivatives as c-Src tyrosine kinase inhibitors
INVENTOR(S): Ple, Patrick
PATENT ASSIGNEE(S): Astrazeneca Ab, Swed.; Astrazeneca Uk Limited
SOURCE: PCT Int. Appl., 124 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2004041829 | A1 | 20040521 | WO 2003-GB4703 | 20031029 |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: EP 2002-292736 A 20021104
EP 2003-290900 A 20030410
OTHER SOURCE(S): MARPAT 140:423698
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

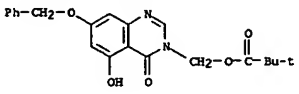
AB The title compds. I [R1 = halo, CF3, cyano, isocyano, NO3, OH, SH, amino, formyl, carboxy, carbamoyl, alkyl, alkenyl, alkynyl, alkoxy, etc.; Z = O, SO, SO2, N(R2)2, or C(R2)2; R2 = H or alkyl; m = 0-3; R3 = halo, CF3, CN, NO2, OH, amino, carboxy, carbamoyl, alkyl, alkenyl, alkynyl, alkoxy, etc.; n =0-3] were prepared as c-Src tyrosine kinase inhibitors in the containment and/or treatment of solid tumor disease. For example, reaction of 4-amino-5-chloro-2,3-methylenedioxypyridine(preparation given) and 4-chloro-7-(3-chloropropoxy)-6-methoxyquinazoline (preparation given) yielded
compound II.

IT **379229-61-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of quinazoline derivs. as c-Src tyrosine kinase inhibitors)

RN 379229-61-5 CAPLUS

CN Propanoic acid, 2,2-dimethyl-, [5-hydroxy-4-oxo-7-(phenylmethoxy)-3(4H)-quinazolinyl]methyl ester (9CI) (CA INDEX NAME)

L4 ANSWER 11 OF 43 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



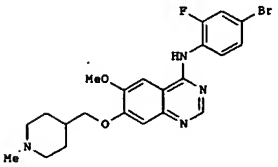
L4 ANSWER 12 OF 43 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:142964 CAPLUS
DOCUMENT NUMBER: 140:175125
TITLE: Combination of ZD6474, an inhibitor of the vascular endothelial growth factor receptor, with radiotherapy in the treatment of cancer
INVENTOR(S): Wedge, Stephen Robert
PATENT ASSIGNEE(S): Astrazeneca AB, Swed.; Astrazeneca UK Limited
SOURCE: PCT Int. Appl., 32 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2004014383 | A1 | 20040219 | WO 2003-GB3388 | 20030805 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2495487 | AA | 20040219 | CA 2003-2495487 | 20030805 |
| EP 1534287 | A1 | 20050601 | EP 2003-784247 | 20030805 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | |

PRIORITY APPLN. INFO.:
GB 2002-18525 A 20020809
GB 2003-7560 A 20030402
WO 2003-GB3388 W 20030805

GI



I

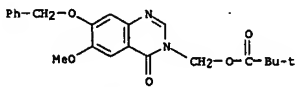
AB The invention discloses a method for the production of an antiangiogenic and/or vascular permeability-reducing effect in a warm-blooded animal, e.g. a human, particularly a method for the treatment of a cancer,

L4 ANSWER 12 OF 43 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

particularly a cancer involving a solid tumor, which comprises the administration of ZD6474 (I) (prepn. described) in combination with ionizing radiation. The invention also discloses the use of ZD6474 in the manuf. of a medicament for use in the prodn. of an antiangiogenic and/or vascular permeability-reducing effect in a warm-blooded animal, e.g. a human, which is being treated with ionizing radiation.

IT 193002-24-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(ZD6474 combination with radiotherapy for treatment of cancer)

RN 193002-24-3 CAPLUS
CN Propanoic acid, 2,2-dimethyl-, [6-methoxy-4-oxo-7-(phenylmethoxy)-3(4H)-quinazolinyl]methyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 13 OF 43 CAPLUS COPYRIGHT 2005 ACS on STN

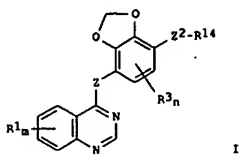
ACCESSION NUMBER: 2004:41281 CAPLUS
DOCUMENT NUMBER: 140:94060
TITLE: Preparation of benzodioxole-containing quinazolines with MAP kinase inhibitory activity for treatment of cancer
INVENTOR(S): Hennequin, Laurent Francois Andre; Foote, Kevin Michael; Gibson, Keith Hopkinson
PATENT ASSIGNEE(S): Astrazeneca AB, Swed.; Astrazeneca UK Limited
SOURCE: PCT Int. Appl., 173 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2004004732 | A1 | 20040115 | WO 2003-GB2874 | 20030704 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| EP 1528925 | A1 | 20050511 | EP 2003-740769 | 20030704 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | |

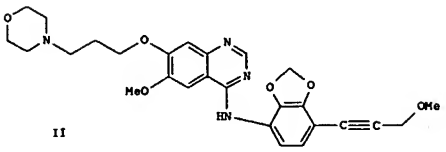
PRIORITY APPLN. INFO.:
GB 2002-15825 A 20020709
GB 2003-12897 A 20030605
WO 2003-GB2874 W 20030704

OTHER SOURCE(S): MARPAT 140:94060
GI

L4 ANSWER 13 OF 43 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



I



II

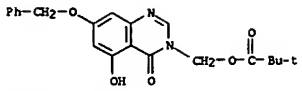
AB The invention concerns benzodioxole-containing quinazolines (shown as I; variables defined below; e.g. II), processes for their preparation, pharmaceutical compns. containing them and their use in the manufacture of a medicament for use as an anti-invasive or anti-proliferative agent in the containment and/or treatment of solid tumor disease (no data). Compds. I possess p44MAP kinase inhibitory activity (no data). Methods of preparation are claimed and .apprx.90 example prepns. are included. For example, II was prepared from N-(7-iodo-1,3-benzodioxol-4-yl)-6-methoxy-7-[3-(morpholin-4-yl)propoxy]quinazolin-4-amine and Me propargyl ether in the presence of bis(triphenylphosphine)palladium(II) chloride, copper iodide and iPr2NH in EtOAc; prepns. of the reactants are also described. For I: Z is O, S, SO, SO2, N(R2) or C(R2)2 (R2 is H or (1-6C)alkyl); m is 0-4; each R1 = halo, trifluoromethyl, cyano, isocyano, nitro, hydroxy, mercapto, amino, formyl, carboxy, carbamoyl, (1-6C)alkyl, (2-8C)alkenyl, (2-8C)alkynyl, etc. N = 0-2; R3 = halo, trifluoromethyl, cyano, nitro, hydroxy, amino, carboxy, carbamoyl, (1-6C)alkyl, (2-8C)alkenyl, (2-8C)alkynyl, (1-6C)alkoxy, etc.; Z2 is C.tplbond.C or C(R13):C(R13) (R13 is H or (1-6C)alkyl); and R14 = halo, cyano, isocyano, formyl, carboxy, (2-8C)alkenyl, (2-8C)alkynyl, (1-6C)alkoxycarbonyl, etc.; addnl. details are given in the claims.

IT 379229-61-5, 7-Benzyloxy-5-hydroxy-3-[(pivaloyloxy)methyl]-3,4-dihydroquinazolin-4-one
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of benzodioxole-containing quinazolines with MAP kinase inhibitory
activity for treatment of cancer)

RN 379229-61-5 CAPLUS

CN Propanoic acid, 2,2-dimethyl-, (5-hydroxy-4-oxo-7-(phenylmethoxy)-3(4H)-quinazolinyl]methyl ester (9CI) (CA INDEX NAME)

L4 ANSWER 13 OF 43 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 14 OF 43 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:532525 CAPLUS
DOCUMENT NUMBER: 139:101142
TITLE: Preparation of substituted quinazoline derivatives as inhibitors of aurora kinases
INVENTOR(S): Jung, Frederic Henri; Pasquet, Georges Rene
PATENT ASSIGNEE(S): Astrazeneca AB, Swed.; Astrazeneca UK Limited
SOURCE: PCT Int. Appl., 175 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2003055491 | A1 | 20030710 | WO 2002-GB5845 | 20021220 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2471577 | AA | 20030710 | CA 2002-2471577 | 20021220 |
| EP 1463506 | A1 | 20041006 | EP 2002-788214 | 20021220 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK | | | | |
| BR 2002015312 | A | 20041207 | BR 2002-15312 | 20021220 |
| US 2005070561 | A1 | 20050331 | US 2004-499684 | 20041117 |
| PRIORITY APPLN. INFO.: | | | EP 2001-403357 A | 20011224 |
| | | | WO 2002-GB5845 W | 20021220 |

OTHER SOURCE(S): MARPAT 139:101142
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

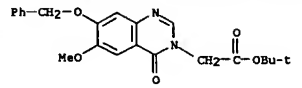
AB Title compds. I [X = O, SOO-2, amino, etc.; R1-4 = H, halo, CN, NO2, CF3, etc.; R5 = pyrazolyl] are prepared For instance, 4-chloro-6-methoxy-7-(3-(morpholinyl)propoxy)quinazoline is heated in the presence of Me (5-amino-1H-pyrazol-3-yl)acetate (pentan-2-ol, HCl, 120°, 2 h) to give Me [5-[(6-methoxy-7-(3-(morpholinyl)propoxy)quinazolin-4-yl)amino]-1H-pyrazol-3-yl]acetate. This intermediate is saponified and condensed with aniline to give II. I are inhibitors of aurora kinase [no data].

IT 557771-41-2P, tert-Butyl 2-(7-[benzyloxy]-6-methoxy-4-oxo-3(4H)-quinazolinyl]acetate
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of substituted quinazoline derivs. as inhibitors of aurora kinases)

RN 557771-41-2 CAPLUS

CN 3(4H)-Quinazolineacetic acid, 6-methoxy-4-oxo-7-(phenylmethoxy)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

L4 ANSWER 14 OF 43 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

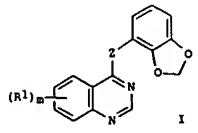


REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 15 OF 43 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:434555 CAPLUS
DOCUMENT NUMBER: 139:22225
TITLE: Preparation of quinazoline compounds for the treatment of T cell mediated diseases
INVENTOR(S): Moore, Nelly Corine; Oldham, Keith
PATENT ASSIGNEE(S): Astrazeneca A.B., Swed.; Astrazeneca UK Limited
SOURCE: PCT Int. Appl., 67 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2003045943 | A1 | 20030605 | WO 2002-GB5182 | 20021120 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| EP 1451180 | A1 | 20040901 | EP 2002-777554 | 20021120 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK | | | | |
| US 2005009850 | A1 | 20050113 | US 2004-496460 | 20040524 |
| PRIORITY APPLN. INFO.: | | | GB 2001-28122 A | 20011123 |
| | | | WO 2002-GB5182 W | 20021120 |

OTHER SOURCE(S): MARPAT 139:22225
GI



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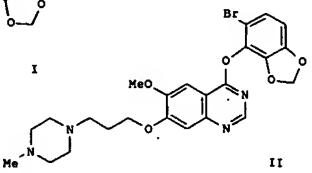


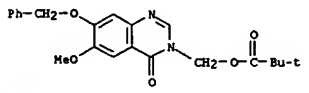
II

L4 ANSWER 15 OF 43 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

AB Quinazoline derivs. of formula I [Z = O, S, SO, SO2, (substituted) CH2; R1 = halo, CF3, CN, nitro, OH, SH, NH2, CHO, alkanoyloxy, heterocyclylalkyloxy, etc.; m = 0-3] are prepared for use in the prevention or treatment of T cell mediated diseases or medical conditions in a warm-blooded animal. Thus, II was prepared and tested for enzyme p56lck inhibition, T cell proliferation inhibition, skin graft rejection inhibition and anti-arthritic activity.

IT 193002-24-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of quinazoline compds. for treatment of T cell mediated diseases)

RN 193002-24-3 CAPLUS
CN Propanoic acid, 2,2-dimethyl-, [6-methoxy-4-oxo-7-(phenylmethoxy)-3(4H)-quinazolinyl]methyl ester (9CI) (CA INDEX NAME)

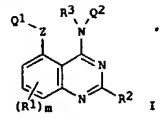


REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 16 OF 43 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:434373 CAPLUS
DOCUMENT NUMBER: 139:6886
TITLE: Preparation of quinazoline derivatives for the treatment of T cell mediated diseases
INVENTOR(S): Moore, Nelly Corine; Oldham, Keith
PATENT ASSIGNEE(S): Astrazeneca A.B., Swed.; Astrazeneca UK Limited
SOURCE: PCT Int. Appl., 217 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2003045395 | A1 | 20030605 | WO 2002-GB5222 | 20021120 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| EP 1450808 | A1 | 20040901 | EP 2002-779708 | 20021120 |
| EP 1450808 | B1 | 20050615 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK | | | | |
| US 2005038050 | A1 | 20050217 | US 2004-496587 | 20040524 |
| PRIORITY APPLN. INFO.: | | | GB 2001-28108 A | 20011123 |
| | | | WO 2002-GB5222 W | 20021120 |

OTHER SOURCE(S): MARPAT 139:6886
GI



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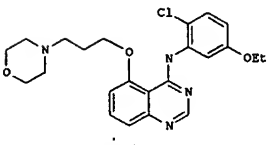


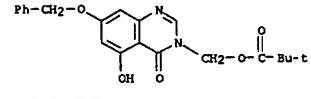
II

L4 ANSWER 16 OF 43 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

AB Title compds. I [m = 0-3; R1 = halo, CF3, CN, NO2, etc.; R2 = H, alkyl; R3 = H, alkyl; Z = bond, O, SO0-2, amino, etc.; Q1 = aryl(alkyl), cycloalkyl, cycloalkenyl, heteroaryl, etc.; Q2 = phenyl] are prepared For instance, 4-[[2-chloro-5-ethoxyphenyl]amino]-5-hydroxy-7-methoxyquinazoline (preparation given) was coupled to 4-(3-hydroxypropyl)morpholine (CH2Cl2, Ph3P, t-BuO2C-N=N-CO2Bu-t) to give II. I are useful for the prevention or treatment of T cell mediated diseases.

IT 379229-61-5P, 7-Benzyloxy-5-hydroxy-3-pivaloyloxymethyl-3,4-dihydroquinazolin-4-one
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(quinazoline derivs. for treatment of T cell mediated diseases)

RN 379229-61-5 CAPLUS
CN Propanoic acid, 2,2-dimethyl-, [5-hydroxy-4-oxo-7-(phenylmethoxy)-3(4H)-quinazolinyl]methyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 17 OF 43 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:434346 CAPLUS
DOCUMENT NUMBER: 139:22222
TITLE: Preparation of arylamino-methoxyquinazolines for the prevention or treatment of T cell-mediated diseases
INVENTOR(S): Moore, Nelly Corine; Oldham, Keith
PATENT ASSIGNEE(S): Astrazeneca A.B., Swed.; Astrazeneca UK Limited
SOURCE: PCT Int. Appl., 127 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2003045364 | A2 | 20030605 | WO 2002-GB5217 | 20021120 |
| WO 2003045364 | A3 | 20030828 | | |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

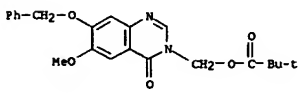
| | | | | |
|---|---|---|---|---|
| EP 1453492 | A2 | 20040908 | EP 2002-777571 | 20021120 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK | | | | |
| US 2005014773 | A1 | 20050120 | US 2004-496464 | 20040524 |
| PRIORITY APPLN. INFO.: | | | GB 2001-28109 | A 20011123 |
| | | | WO 2002-GB5217 | W 20021120 |

OTHER SOURCE(S): MARPAT 139:22222
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [m = 0-3; R1 = halo, CF3, CN, NCO, NO2, OH, etc.; R2 = H, alkyl; R3 = halo, CF3, CN, NO2, OH, amino, carboxy, etc.] are prepared For instance, 4-chloro-6-methoxy-7-(3-morpholinopropoxy)quinazoline (preparation given) is coupled to 2,3-methylenedioxyaniline (sec-pentanol, HCl, IPA) to give II as the bis•HCl salt. I are useful for the prevention or treatment of T cell mediated diseases or medical conditions in a warm-blooded animal.
IT 193002-24-3P, 7-Benzyloxy-6-methoxy-3-pivaloyloxymethyl-3,4-dihydroquinazolin-4-one
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of arylamino-methoxyquinazolines for the prevention or treatment of T cell-mediated diseases)
RN 193002-24-3 CAPLUS

L4 ANSWER 17 OF 43 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
CN Propanoic acid, 2,2-dimethyl-, [6-methoxy-4-oxo-7-(phenylmethoxy)-3(4H)-quinazolinyl]methyl ester (9CI) (CA INDEX NAME)




L4 ANSWER 18 OF 43 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:376831 CAPLUS
DOCUMENT NUMBER: 138:385442
TITLE: Preparation of (anilino)quinazolines as antitumor agents
INVENTOR(S): Hennequin, Laurent Francois Andre; Kettle, Jason Grant; Pass, Martin; Bradbury, Robert Hugh
PATENT ASSIGNEE(S): Astrazeneca AB, Swed.; Astrazeneca UK Limited
SOURCE: PCT Int. Appl., 275 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2003040109 | A2 | 20030515 | WO 2002-GB4932 | 20021031 |
| WO 2003040109 | A3 | 20030626 | | |

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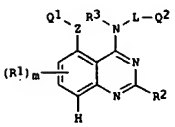
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

| | | | | |
|---|---|---|---|---|
| CA 2465100 | AA | 20030515 | CA 2002-2465100 | 20021031 |
| EP 1444211 | A2 | 20040811 | EP 2002-774961 | 20021031 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK | | | | |
| BR 2002013843 | A | 20040831 | BR 2002-13843 | 20021031 |
| JP 2005511603 | T2 | 20050428 | JP 2003-542155 | 20021031 |
| US 2005054662 | A1 | 20050310 | US 2004-494388 | 20041001 |
| PRIORITY APPLN. INFO.: | | | GB 2001-26433 | A 20011103 |
| | | | WO 2002-GB4932 | W 20021031 |

OTHER SOURCE(S): MARPAT 138:385442
GI

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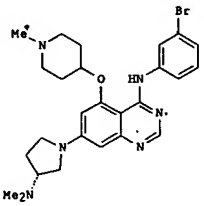
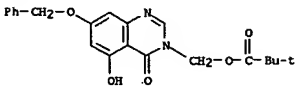


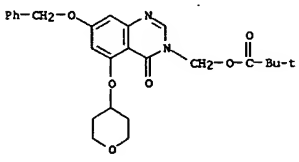

II

L4 ANSWER 18 OF 43 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
AB Title compds. I [wherein m = 0-2; n = 1-2; L = a bond or [C(R22)2]n; R1 = halo, CF3, CN, NC, NO2, OH, SH, NH2, CHO, CO2H, CONH2, or (un)substituted alkyl(oxy), alkenyl(oxy), alkynyl(oxy), alkylthio, alkylsulfinyl, alkylsulfonyl, (di)alkylamino, alkoxycarbonyl, (di)alkylcarbamoyl, alkanoyl(oxy), (alkyl)alkanoylamino, (alkyl)alkenoylamino, (alkyl)alkynoylamino, (di)alkylsulfamoyl, (alkyl)alkanesulfonylamino, or Q3X1; or (R1)m = alkylenedioxy; with the proviso that adjacent alkylene C atoms within a R1 substituent are optionally interrupted by O, S, SO, SO2, NR5, CO, CHOR5, CONR5, NR5CO, SO2NR5, NR5SO2, CH=CH, or C.tplbond.C; R2 = H; R3, R4, R5, R11, R12, and R22 = independently H or alkyl; Q1 and Q3 = independently (un)substituted (hetero)aryl(alkyl), cycloalkyl(alkyl), cycloalkenyl(alkyl), or heterocyclyl(alkyl); with the proviso that adjacent alkylene C atoms within the Q1Z group are optionally interrupted by O, S, SO, SO2, NR12, CO, CHOR12, CONR12, NR12CO, SO2NR12, NR12SO2, CH=CH, or C.tplbond.C; Q2 = (un)substituted Ph, bicyclic (hetero)aryl, or bicyclic heterocyclyl; X1 = a bond, O, S, SO, SO2, NR4, CO, CHOR4, CONR4, NR4CO, SO2NR4, NR4SO2, OC(R4)2, SC(R4)2, or NR4C(R4)2; Z = a bond, O, S, SO, SO2, NR11, CO, CHOR11, CONR11, NR11CO, SO2NR11, NR11SO2, OC(R11)2, SC(R11)2, or NR11C(R11)2; and pharmaceutically acceptable salts thereof] were prepared for use in the prevention or treatment of tumors which are sensitive to inhibition of erbB receptor tyrosine kinases. For example, coupling of 3-(R)-(+)-dimethylaminopyrrolidine with 3,4-dihydro-5-hydroxy-7-fluoroquinazolin-4-one•CF3CO2H in NMP gave the pyrrolidinylquinazolinone (41%). Addition of chloromethyl pivalate in the presence of NaH in DMF afforded the 3-substituted derivative (62%), which was condensed with 4-hydroxy-N-methylpiperidine using PPh3 and di-tert-Bu azodicarboxylate in DCM to give the piperidinyloxyquinazolinone (77%). Deprotection (66%) using NH3 in MeOH, followed by chlorination with POCl3 and di-isopropylethylamine in dichloroethane provided 4-chloro-7-(3-(R)-dimethylaminopyrrolidin-1-yl)-5-(1-methylpiperidin-4-yloxy)quinazoline (81%). Coupling of the chloroquinazoline with 3-bromoaniline in the presence of HCl and IPA in dioxane yielded II•HCl (43%). The biol. activity of the example compds. was assessed in five assays. Thus, I inhibited the phosphorylation of a tyrosine-containing polypeptide substrate by epidermal growth factor receptor (EGFR) kinase, erbB2 kinase, and erbB4 kinase with IC50 values in the range of 0.001 μM - 10 μM. I also inhibited the proliferation of both human naso-pharyngeal carcinoma KB cells and non-neoplastic epithelial H16N-2 cells with IC50 values in the range 0.001 μM - 20 μM. In addition, I inhibited the growth of colorectal adenocarcinoma LoVo and human mammary carcinoma BT-474 tumor cell xenografts in vivo with activities in the range of 1 mg/kg/day to 200 mg/kg/day with no physiol. unacceptable toxicity at the ED.
IT 379229-61-5P, 7-Benzyloxy-5-hydroxy-3-pivaloyloxymethyl-3,4-dihydroquinazolin-4-one 525593-06-0P, 7-Benzyloxy-3-pivaloyloxymethyl-5-[(tetrahydropyran-4-yl)oxy]-3,4-dihydroquinazolin-4-one 525593-07-1P, 7-Benzyloxy-5-(1-methylpiperidin-4-yloxy)-3-pivaloyloxymethyl-3,4-dihydroquinazolin-4-one 525593-08-2P, 7-Benzyloxy-3-pivaloyloxymethyl-5-[(tetrahydrofuran-3-yl)oxy]-3,4-dihydroquinazolin-4-one 525593-09-3P, 7-Benzyloxy-5-cyclopentyloxy-3-pivaloyloxymethyl-3,4-dihydroquinazolin-4-one
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of (anilino)quinazolines as erbB receptor tyrosine kinase inhibitors for treatment of cancer)
RN 379229-61-5 CAPLUS
CN Propanoic acid, 2,2-dimethyl-, [5-hydroxy-4-oxo-7-(phenylmethoxy)-3(4H)-quinazolinyl]methyl ester (9CI) (CA INDEX NAME)

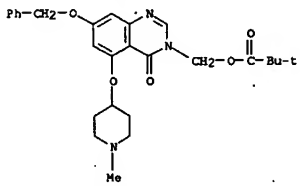
L4 ANSWER 18 OF 43 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



RN 525593-06-0 CAPLUS
CN Propanoic acid, 2,2-dimethyl-, [4-oxo-7-(phenylmethoxy)-5-[(tetrahydro-2H-pyran-4-yl)oxy]-3(4H)-quinazolinyl]methyl ester (9CI) (CA INDEX NAME)

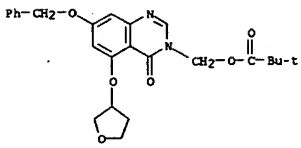


RN 525593-07-1 CAPLUS
CN Propanoic acid, 2,2-dimethyl-, [5-[(1-methyl-4-piperidinyl)oxy]-4-oxo-7-(phenylmethoxy)-3(4H)-quinazolinyl]methyl ester (9CI) (CA INDEX NAME)

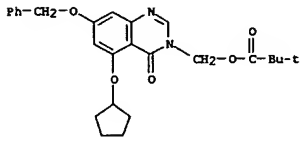


RN 525593-08-2 CAPLUS
CN Propanoic acid, 2,2-dimethyl-, [4-oxo-7-(phenylmethoxy)-5-[(tetrahydro-3-furanyl)oxy]-3(4H)-quinazolinyl]methyl ester (9CI) (CA INDEX NAME)

L4 ANSWER 18 OF 43 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



RN 525593-09-3 CAPLUS
CN Propanoic acid, 2,2-dimethyl-, [5-(cyclopentyloxy)-4-oxo-7-(phenylmethoxy)-3(4H)-quinazolinyl]methyl ester (9CI) (CA INDEX NAME)



L4 ANSWER 19 OF 43 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:376644 CAPLUS
DOCUMENT NUMBER: 138:379206
TITLE: Combination cancer therapy comprising ZD6474 and a taxane
INVENTOR(S): Wedge, Stephen Robert
PATENT ASSIGNEE(S): Astrazeneca AB, Swed.; Astrazeneca UK Limited
SOURCE: PCT Int. Appl., 35 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

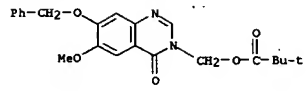
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2003039551 | A1 | 20030515 | WO 2002-GB5021 | 20021106 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2464758 | AA | 20030515 | CA 2002-2464758 | 20021106 |
| EP 1446124 | A1 | 20040818 | EP 2002-772624 | 20021106 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK | | | | |
| BR 2002013906 | A | 20040831 | BR 2002-13906 | 20021106 |
| JP 2005511597 | T2 | 20050428 | JP 2003-541842 | 20021106 |
| US 2005043395 | A1 | 20050224 | US 2004-494704 | 20041019 |
| PRIORITY APPLN. INFO.: | | | GB 2001-26879 A | 20011108 |
| | | | WO 2002-GB5021 W | 20021106 |

AB The invention provides a method for the production of an antiangiogenic and/or vascular permeability-reducing effect in a warm-blooded animal such as a human, particularly a method for the treatment of a cancer involving a solid tumor, which comprises the administration of ZD6474 [4-(4-bromo-2-fluoroanilino)-6-methoxy-7-(1-methylpiperidin-4-ylmethoxy)quinazoline; preparation described] in combination with a taxane. The invention also provides a pharmaceutical composition comprising ZD6474 and a taxane; a combination product comprising ZD6474 and a taxane for use in a method of treatment of a human or animal body by therapy; a kit comprising ZD6474 and a taxane; the use of ZD6474 and a taxane in the manufacture of a medicament for use in the production of an antiangiogenic and/or vascular permeability-reducing effect in a warm-blooded animal such as a human which is optionally being treated with ionizing radiation.

IT **193002-24-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(ZD6474-taxane combination for cancer therapy)

RN 193002-24-3 CAPLUS
CN Propanoic acid, 2,2-dimethyl-, [6-methoxy-4-oxo-7-(phenylmethoxy)-3(4H)-quinazolinyl]methyl ester (9CI) (CA INDEX NAME)

L4 ANSWER 19 OF 43 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

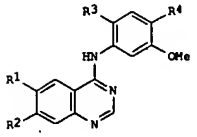


REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 20 OF 43 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:888721 CAPLUS
DOCUMENT NUMBER: 137:384856
TITLE: Preparation of 4-anilinoquinazolines as antitumor agents
INVENTOR(S): Hennequin, Laurent Francois Andre; Ple, Patrick
PATENT ASSIGNEE(S): Astrazeneca AB, Swed.; Astrazeneca UK Limited
SOURCE: PCT Int. Appl., 78 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2002092578 | A1 | 20021121 | WO 2002-GB2124 | 20020508 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |

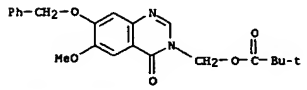
PRIORITY APPLN. INFO.: EP 2001-401222 A 20010514
OTHER SOURCE(S): MARPAT 137:384856
GI



I

AB The title compds. [I; R1 = H, alkoxy and R2 = X1Q1 (wherein X1 = O, S, SO, etc.; Q1 = heteroaryl, heteroarylalkyl, heterocyclyl, etc.), X2R5 (wherein X2 = O, NH, Nalkyl; R5 = hydroxyalkyl, alkoxyalkyl, aminoalkyl, etc.); or R2 = H, alkoxy and R1 = X1Q1, X2R5; R3, R4 = Cl, Br, I], useful as anti-invasive agents in the containment and/or treatment of solid tumor disease, were prepared and formulated. E.g., a multi-step synthesis of I.2HCl [R1 = OMe; R2 = N-methylpiperidin-4-ylmethoxy; R3, R4 = Cl], starting from Et piperidine-4-carboxylate, was given. Biol. activity of compds. I was tested in 4 tests. Thus, the compds. I showed IC50 of 0.001-10 μM in in vitro c-Src tyrosine kinase assay.
IT 193002-24-3P, 7-Benzyloxy-6-methoxy-3-pivaloyloxymethyl-3,4-dihydroquinazolin-4-one
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT

L4 ANSWER 20 OF 43 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
(Reactant or reagent)
(prepn. of 4-anilinoquinazolines as antitumor agents)
RN 193002-24-3 CAPLUS
CN Propanoic acid, 2,2-dimethyl-, [6-methoxy-4-oxo-7-(phenylmethoxy)-3(4H)-quinazolinyl]methyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 21 OF 43 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:888720 CAPLUS
DOCUMENT NUMBER: 137:384855
TITLE: Preparation of 4-anilinoquinazolines as antitumor agents
INVENTOR(S): Hennequin, Laurent Francois Andre; Ple, Patrick
PATENT ASSIGNEE(S): Astrazeneca AB, Swed.; Astrazeneca UK Limited
SOURCE: PCT Int. Appl., 96 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2002092577 | A1 | 20021121 | WO 2002-GB2117 | 20020508 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |

PRIORITY APPLN. INFO.: EP 2001-401223 A 20010514
OTHER SOURCE(S): MARPAT 137:384855
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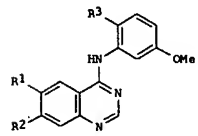
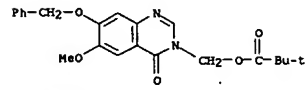


I

AB The title compds. [I; R1 = H, alkoxy and R2 = X1Q1 (wherein X1 = O, S, SO, etc.; Q1 = heteroaryl, heteroarylalkyl, heterocyclyl, etc.), X2R5 (wherein X2 = O, NH, Nalkyl; R5 = hydroxyalkyl, alkoxyalkyl, aminoalkyl, etc.); or R2 = H, alkoxy and R1 = X1Q1, X2R5; R3 = Cl, Br, I], useful as anti-invasive agents in the containment and/or treatment of solid tumor disease, were prepared and formulated. E.g., a multi-step synthesis of I [R1 = OMe; R2 = N-methylpiperidin-4-ylmethoxy; R3 = Cl], starting from Et piperidine-4-carboxylate, was given. Biol. activity of compds. I was tested in 4 tests. Thus, the compds. I showed IC50 of 0.001-10 μM in in vitro c-Src tyrosine kinase assay.
IT 193002-24-3P, 7-Benzyloxy-6-methoxy-3-pivaloyloxymethyl-3,4-dihydroquinazolin-4-one
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of 4-anilinoquinazolines as antitumor agents)
RN 193002-24-3 CAPLUS
CN Propanoic acid, 2,2-dimethyl-, [6-methoxy-4-oxo-7-(phenylmethoxy)-3(4H)-

L4 ANSWER 21 OF 43 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
quinazolinyl]methyl ester (9CI) (CA INDEX NAME)

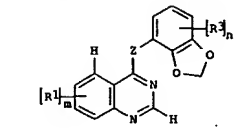


REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 22 OF 43 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:832791 CAPLUS
DOCUMENT NUMBER: 137:337908
TITLE: Preparation of antitumor quinazolines
INVENTOR(S): Ple, Patrick
PATENT ASSIGNEE(S): Astrazeneca AB, Swed.; Astrazeneca UK Limited
SOURCE: PCT Int. Appl., 73 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2002085895 | A1 | 20021031 | WO 2002-GB1734 | 20020415 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| EP 1381599 | A1 | 20040121 | EP 2002-718343 | 20020415 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | | |
| JP 2004525984 | T2 | 20040826 | JP 2002-583422 | 20020415 |
| US 2004138240 | A1 | 20040715 | US 2003-475016 | 20031016 |
| PRIORITY APPLN. INFO.: | | | EP 2001-401007 A | 20010419 |
| | | | WO 2002-GB1734 W | 20020415 |

OTHER SOURCE(S): MARPAT 137:337908
GI



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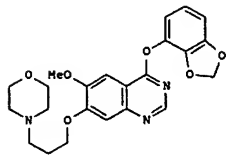
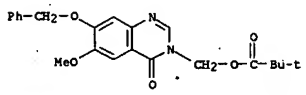


II

AB The title compds. [I; Z = O, S, SO, etc.; m = 0-3; R1 = halo, CF3, CN, etc.; n = 0-3; R3 = halo, CF3, CN, etc.], useful in the manufacture of a medicament for use as an anti-invasive agent in the containment and/or treatment of solid tumor disease, were prepared Thus, a multi-step synthesis of the quinazoline II, starting from 2-amino-4-benzyloxy-5-methoxybenzamide, was given. The compds. I show IC50 in the range of 0.001-10 μM in in vitro c-Src kinase assay.

IT 193002-24-3P, 7-Benzyloxy-6-methoxy-3-pivaloyloxymethyl-3,4-dihydroquinazolin-4-one
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of antitumor quinazolines)

RN 193002-24-3 CAPLUS
CN Propanoic acid, 2,2-dimethyl-, [6-methoxy-4-oxo-7-(phenylmethoxy)-3(4H)-quinazolinyl]methyl ester (9CI) (CA INDEX NAME)

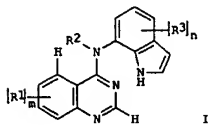


REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 23 OF 43 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:332187 CAPLUS
DOCUMENT NUMBER: 136:340694
TITLE: Preparation of 4-(indol-7-ylamino)quinazolines as antitumor agents
INVENTOR(S): Lambert, Christine Marie-Paul; Ple, Patrick
PATENT ASSIGNEE(S): Astrazeneca AB, Swed.; Astrazeneca UK Limited
SOURCE: PCT Int. Appl., 70 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2002034744 | A1 | 20020502 | WO 2001-GB4674 | 20011019 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| AU 2002012436 | A5 | 20020506 | AU 2002-12436 | 20011019 |
| EP 1332141 | A1 | 20030806 | EP 2001-980640 | 20011019 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | | |
| JP 2004512335 | T2 | 20040422 | JP 2002-537735 | 20011019 |
| US 2004063733 | A1 | 20040401 | US 2003-415053 | 20031022 |
| PRIORITY APPLN. INFO.: | | | EP 2000-402962 A | 20001025 |
| | | | WO 2001-GB4674 W | 20011019 |

OTHER SOURCE(S): MARPAT 136:340694
GI



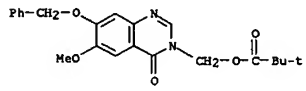
I

AB The title compds. [I; m = 0-3; R1 = halo, CF3, CN, etc.; R2 = H, alkyl; n = 0-3; R3 = halo, CF3, CN, etc.] and their pharmaceutically acceptable salts, useful in the manufacture of a medicament for use as an anti-invasive agent in the containment and/or treatment of solid tumor disease, were prepared E.g., a multi-step synthesis of I [m = 2; R1 = 6-OMe; R1 = 7-(3-morpholinopropoxy); R2 = H; n = 2; R3 = 2,3-Me2], was given. The compds. I were tested for c-Src tyrosine kinase inhibition, and in general their activity may be demonstrated by IC50 in the range, for example, 0.001-10 μM.

IT 193002-24-3P, 7-Benzyloxy-6-methoxy-3-pivaloyloxymethyl-3,4-dihydroquinazolin-4-one

L4 ANSWER 23 OF 43 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of 4-(indol-7-ylamino)quinazolines as antitumor agents)

RN 193002-24-3 CAPLUS
CN Propanoic acid, 2,2-dimethyl-, [6-methoxy-4-oxo-7-(phenylmethoxy)-3(4H)-quinazolinyl]methyl ester (9CI) (CA INDEX NAME)

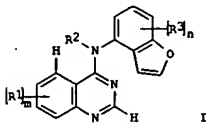


REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 24 OF 43 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:293648 CAPLUS
DOCUMENT NUMBER: 136:325554
TITLE: Preparation of 4-(4-benzofuranylamino)quinazolines as c-Src tyrosine kinase inhibitors
INVENTOR(S): Lambert, Christine Marie-Paul; Ple, Patrick
PATENT ASSIGNEE(S): Astrazeneca AB, Swed.; Astrazeneca UK Limited
SOURCE: PCT Int. Appl., 81 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2002030926 | A1 | 20020418 | WO 2001-GB4497 | 20011009 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| AU 2001092137 | A5 | 20020422 | AU 2001-92137 | 20011009 |
| EP 1326860 | A1 | 20030716 | EP 2001-972363 | 20011009 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | | |
| JP 2004511480 | T2 | 20040415 | JP 2002-534312 | 20011009 |
| US 2004044015 | A1 | 20040304 | US 2003-399017 | 20030410 |
| PRIORITY APPLN. INFO.: | | | EP 2000-402845 A | 20001013 |
| | | | WO 2001-GB4497 W | 20011009 |

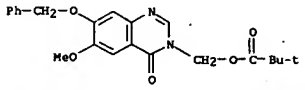
OTHER SOURCE(S): MARPAT 136:325554
GI



I

AB The title compds. [I; m = 0-3; R1 = halo, CF3, CN, etc.; R2 = H, alkyl; n = 0-3; R3 = halo, CF3, CN, etc.], useful as an anti-invasive agent in the containment and/or treatment of solid tumor disease, were prepared Thus, reacting 4-chloro-6-methoxy-7-[3-(4-methylpiperazin-1-yl)propoxy]quinazoline with 4-aminobenzofuran (prepns. given) in the presence of HCl/iso-PrOH afforded I.2HCl [m = 2; R1 = 6-methoxy; R1 = 7-[3-(4-methylpiperazin-1-yl)propoxy]; R2, R3 = H]. Biol. data were

L4 ANSWER 24 OF 43 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
given.
IT 193002-24-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of 4-(4-benzofuranylamino)quinazolines as c-Src tyrosine kinase inhibitors)
RN 193002-24-3 CAPLUS
CN Propanoic acid, 2,2-dimethyl-, [6-methoxy-4-oxo-7-(phenylmethoxy)-3(4H)-quinazolinyl]methyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 25 OF 43 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:293646 CAPLUS
DOCUMENT NUMBER: 136:325553
TITLE: Preparation of 4-(7-benzofuranylamino)quinazolines with antitumor activity
INVENTOR(S): Lambert, Christine Marie Paul; Ple, Patrick
PATENT ASSIGNEE(S): Astrazeneca AB, Swed.; Astrazeneca UK Limited
SOURCE: PCT Int. Appl., 92 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2002030924 | A1 | 20020418 | WO 2001-GB4498 | 20011009 |
| WO 2002030924 | C2 | 20030522 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| AU 2001092138 | A5 | 20020422 | AU 2001-92138 | 20011009 |
| EP 1326859 | A1 | 20030716 | EP 2001-972364 | 20011009 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | | |
| JP 2004511479 | T2 | 20040415 | JP 2002-534310 | 20011009 |
| US 2004048881 | A1 | 20040311 | US 2003-398793 | 20030408 |
| US 6849625 | B2 | 20050201 | | |
| PRIORITY APPLN. INFO.: | | | EP 2000-402844 A | 20001013 |
| | | | WO 2001-GB4498 W | 20011009 |

OTHER SOURCE(S): MARPAT 136:325553
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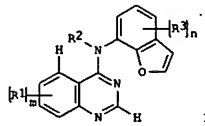
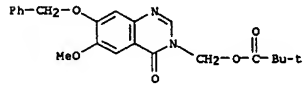


I

AB The title compds. [I; m = 0-3; R1 = halo, CF3, CN, etc.; R2 = H, alkyl; n = 0-3; R3 = halo, CF3, CN, etc.], useful as anti-invasive agents in the containment and/or treatment of solid tumor disease, were prepared and formulated. Thus, reacting 4-chloro-6-methoxy-7-[3-(4-methylpiperazin-1-yl)propoxy]quinazoline with 7-aminobenzofuran (prepns. given) in the presence of HCl/iso-PrOH afforded I.2HCl [m = 2; R1 = 6-MeO; R1 =

L4 ANSWER 25 OF 43 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
7-[3-(4-methylpiperazin-1-yl)propoxy]; R2, R3 = H]. Biol. data for compds. I (i.e., as c-Src tyrosine kinase inhibitors) were given.
IT 193002-24-3P, 7-Benzyloxy-6-methoxy-3-pivaloyloxymethyl-3,4-dihydroquinazolin-4-one
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of 4-(7-benzofuranylamino)quinazolines with antitumor activity)
RN 193002-24-3 CAPLUS
CN Propanoic acid, 2,2-dimethyl-, [6-methoxy-4-oxo-7-(phenylmethoxy)-3(4H)-quinazolinyl]methyl ester (9CI) (CA INDEX NAME)

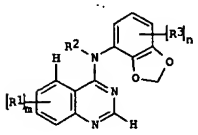


REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 26 OF 43 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:157764 CAPLUS
DOCUMENT NUMBER: 136:200201
TITLE: Preparation of quinazolines as an anti-invasive agent in the containment and/or treatment of solid tumor disease
INVENTOR(S): Hennequin, Laurent Francois Andre; Ple, Patrick; Lambert, Christine Marie Paul
PATENT ASSIGNEE(S): Astrazeneca AB, Swed.; Astrazeneca UK Limited
SOURCE: PCT Int. Appl., 138 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2002016352 | A1 | 20020228 | WO 2001-GB3649 | 20010815 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2419301 | AA | 20020228 | CA 2001-2419301 | 20010815 |
| AU 2001078609 | A5 | 20020304 | AU 2001-78609 | 20010815 |
| EP 1313727 | A1 | 20030528 | EP 2001-956688 | 20010815 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | | |
| BR 2001013358 | A | 20030701 | BR 2001-13358 | 20010815 |
| JP 2004506732 | T2 | 20040304 | JP 2002-521453 | 20010815 |
| NZ 523702 | A | 20040827 | NZ 2001-523702 | 20010815 |
| EE 200300071 | A | 20041215 | EE 2003-71 | 20010815 |
| ZA 2003000569 | A | 20040421 | ZA 2003-569 | 20030121 |
| US 2004034046 | A1 | 20040219 | US 2003-344678 | 20030214 |
| NO 2003000795 | A | 20030404 | NO 2003-795 | 20030220 |
| PRIORITY APPLN. INFO.: | | | EP 2000-402320 A | 20000821 |
| | | | EP 2001-401006 A | 20010419 |
| | | | WO 2001-GB3649 W | 20010815 |

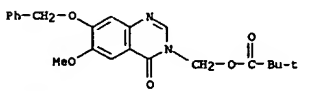
OTHER SOURCE(S): MARPAT 136:200201
GI



I

L4 ANSWER 26 OF 43 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

AB The title compds. [I; m, n = 0-3; R1 = halo, CF3, CN, etc.; R2 = H, alkyl; R3 = halo, CF3, CN, etc.] and their salts, useful in the manufacture of a medicament for use as an anti-invasive agent in the containment and/or treatment of solid tumor disease, were prepared and formulated. E.g., a multi-step synthesis of I [R1 = 7-(3-morpholinopropoxy); m = 1; R2, R3 = H] was given. The compds. I showed IC50's of 0.001-10 μM against c-src tyrosine kinase.
IT 193002-24-3P, 7-Benzyloxy-6-methoxy-3-pivaloyloxymethyl-3,4-dihydroquinazolin-4-one
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of quinazolines as an anti-invasive agent in the containment and/or treatment of solid tumor disease)
RN 193002-24-3 CAPLUS
CN Propanoic acid, 2,2-dimethyl-, [6-methoxy-4-oxo-7-(phenylmethoxy)-3(4H)-quinazolinyl]methyl ester (9CI) (CA INDEX NAME)

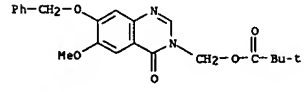


REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 27 OF 43 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:31424 CAPLUS
DOCUMENT NUMBER: 136:102393
TITLE: Preparation of quinazolinylureas for treatment of solid tumors.
PATENT ASSIGNEE(S): Astrazeneca Ab, Swed.; Astrazeneca Uk Ltd.
SOURCE: PCT Int. Appl., 149 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2002002534 | A1 | 20020110 | WO 2001-GB2874 | 20010628 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| PRIORITY APPLN. INFO.: | | | EP 2000-401897 A | 20000703 |

OTHER SOURCE(S): MARPAT 136:102393
AB Use of Q1R2NC(:Z)NR3Q2 [Q1 = (substituted) (fused) quinazolinyl, quinolinyl, etc.; Q2 = (substituted) aryl, aralkyl, arylcycloalkyl, heteroaryl, heteroarylalkyl; R2, R3 = H, alkyl; R2R3 = CH2, CH2CH2, (CH2)3] as antiinvasive agents in the containment and/or treatment of solid tumor disease is claimed. Thus, 2,6-dichlorophenyl isocyanate was added to a solution of 4-amino-6-methoxy-7-(N-methylpiperidin-4-ylmethoxy)quinazoline (preparation given) in CH2Cl2/DMF followed by stirring to give 1-(2,6-dichlorophenyl)-3-[6-methoxy-7-(N-methylpiperidin-4-ylmethoxy)quinazolin-4-yl]urea. Title compds. inhibited proliferation of NIH 3T3 fibroblasts with IC50 in the range, for example, of 0.001-10 μM.
IT 193002-24-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of quinazolinylureas for treatment of solid tumors)
RN 193002-24-3 CAPLUS
CN Propanoic acid, 2,2-dimethyl-, [6-methoxy-4-oxo-7-(phenylmethoxy)-3(4H)-quinazolinyl]methyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 28 OF 43 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:904160 CAPLUS
DOCUMENT NUMBER: 136:20087
TITLE: Preparation of 4-anilinoquinazoline derivatives for the treatment of tumors
INVENTOR(S): Hennequin, Laurent Francois Andre; Ple, Patrick
PATENT ASSIGNEE(S): Astrazeneca Ab, Swed.; Astrazeneca Uk Limited
SOURCE: PCT Int. Appl., 234 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2001094341 | A1 | 20011213 | WO 2001-GB2424 | 20010601 |
| WO 2001094341 | C2 | 20030417 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2407371 | AA | 20011213 | CA 2001-2407371 | 20010601 |
| EP 1292594 | A1 | 20030319 | EP 2001-934176 | 20010601 |
| EP 1292594 | B1 | 20040901 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | | |
| BR 2001011335 | A | 20030610 | BR 2001-11335 | 20010601 |
| JP 2003535859 | T2 | 20031202 | JP 2002-501890 | 20010601 |
| EE 200200673 | A | 20040615 | EE 2002-673 | 20010601 |
| NZ 522204 | A | 20040730 | NZ 2001-522204 | 20010601 |
| AT 275145 | E | 20040915 | AT 2001-934176 | 20010601 |
| ES 2225545 | T3 | 20050316 | ES 2001-934176 | 20010601 |
| US 2004214841 | A1 | 20041028 | US 2002-275382 | 20021105 |
| ZA 2002009122 | A | 20040209 | ZA 2002-9122 | 20021108 |
| BG 107332 | A | 20030731 | BG 2002-107332 | 20021128 |
| NO 2002005792 | A | 20021202 | NO 2002-5792 | 20021202 |
| HK 1053115 | A1 | 20050408 | HK 2003-105395 | 20030725 |
| PRIORITY APPLN. INFO.: | | | EP 2000-401581 A | 20000606 |
| | | | EP 2001-400297 A | 20010207 |
| | | | EP 2001-400565 A | 20010305 |
| | | | WO 2001-GB2424 W | 20010601 |

OTHER SOURCE(S): MARPAT 136:20087
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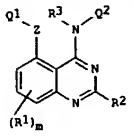
L4 ANSWER 28 OF 43 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



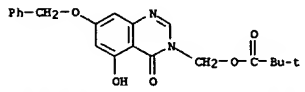
I

AB The invention concerns quinazoline derivs. (I; e.g. 4-(2-chloro-5-methoxyanilino)-7-methoxy-5-(3-morpholinopropoxy)quinazoline (1)), processes for their preparation, pharmaceutical compns. containing them and their use in the manufacture of a medicament for use as an anti-invasive agent in the containment and/or treatment of solid tumor disease. Although biol. assay methods are described, no test results are reported. It is believed that the antitumor activity is due to inhibition of one or more of the non-receptor tyrosine-specific protein kinases of the Src family that are involved in the signal transduction steps that lead to the invasiveness and migratory ability of metastasizing tumor cells. In I, according to the 1st claim, m = 0-3; each R1 = halo, trifluoromethyl, cyano, isocyano, nitro, hydroxy, mercapto, amino, formyl, carboxy, carbamoyl, (1-6C)alkyl, (2-8C)alkenyl, (2-8C)alkynyl, (1-6C)alkoxy, (2-6C)alkenyloxy, (2-6C)alkynyloxy, (1-6C)alkylthio, (1-6C)alkylsulfinyl, (1-6C)alkylsulfonyl, (1-6C)alkylamino, di[(1-6C)alkyl]amino, (1-6C)alkoxycarbonyl, N-(1-6C)alkylcarbamoyl, N,N-di[(1-6C)alkyl]carbamoyl, (2-6C)alkanoyl, (2-6C)alkanoyloxy, (2-6C)alkanoylamino, N-(1-6C)alkyl-(2-6C)alkanoylamino, (3-6C)alkenoylamino, N-(1-6C)alkyl-(3-6C)alkenoylamino, (3-6C)alkynoylamino, N-(1-6C)alkyl-(3-6C)alkynoylamino, N-(1-6C)alkylsulfamoyl, N,N-di[(1-6C)alkyl]sulfamoyl, (1-6C)alkanesulfonylamino and N-(1-6C)alkyl-(1-6C)alkanesulfonylamino, or Q3-X1- (X1 = direct bond, O, S, SO, SO2, N(R4), CO, CH(OR4), CON(R4), N(R4)CO, SO2N(R4), N(R4)SO2, OC(R4)2, SC(R4)2 and N(R4)C(R4)2 (R4 = H or (1-6C)alkyl) and Q3 = aryl, aryl-(1-6C)alkyl, (3-7C)cycloalkyl, (3-7C)cycloalkyl-, (1-6C)alkyl, (3-7C)cycloalkenyl, (3-7C)cycloalkenyl-(1-6C)alkyl, heteroaryl, heteroaryl-(1-6C)alkyl, heterocyclyl or heterocyclyl-(1-6C)alkyl), or (R1)m is (1-3C)alkylenedioxy, with addnl. optional substitution and/or insertion possible. R2 = H or (1-6C)alkyl; R3 = H or (1-6C)alkyl; Z = direct bond, O, S, SO, SO2, N(R11), CO, CH(OR11), CON(R11), N(R11)CO, SO2N(R11), N(R11)SO2, OC(R11)2, SC(R11)2 and N(R11)C(R11)2 (R11 = H, or (1-6C)alkyl). Q1 = aryl, aryl-(1-6C)alkyl, (3-7C)cycloalkyl, (3-7C)cycloalkyl-(1-6C)alkyl, (3-7C)cycloalkenyl, (3-7C)cycloalkenyl-(1-6C)alkyl, heteroaryl, heteroaryl-(1-6C)alkyl, heterocyclyl or heterocyclyl-(1-6C)alkyl, or, when Z is a direct bond or O, Q1 may be (1-6C)alkyl, (2-8C)alkenyl, (2-8C)alkynyl, halo-(1-6C)alkyl, hydroxy-(1-6C)alkyl, (1-6C)alkoxy-(1-6C)alkyl, cyano-(1-6C)alkyl, amino-(1-6C)alkyl, (1-6C)alkylamino-(1-6C)alkyl, di[(1-6C)alkyl]amino-(1-6C)alkyl, (1-6C)alkylthio-(1-6C)alkyl, (1-6C)alkylsulfinyl-(1-6C)alkyl or (1-6C)alkylsulfonyl-(1-6C)alkyl, with addnl. optional substitution and/or insertion possible. Q2 = substituted Ph. More than 50 example prepns. are included. For example, 1 was obtained by adding di-tert-Bu azodicarboxylate (0.208 g) dropwise to a stirred mixt. of 4-(2-chloro-5-methoxyanilino)-5-hydroxy-7-methoxyquinazoline (0.2 g), 4-(3-hydroxypropyl)morpholine, PPh3 (0.237 g) and CH2Cl2 (3 mL). The reaction mixt. was stirred at ambient temp. for 1 h.

IT **379229-61-5P**, 7-Benzyloxy-5-hydroxy-3-pivaloyloxymethyl-3,4-dihydroquinazolin-4-one
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of anilinoquinazoline derivs. for treatment of tumors)

RN 379229-61-5 CAPLUS

CN Propanoic acid, 2,2-dimethyl-, [5-hydroxy-4-oxo-7-(phenylmethoxy)-3(4H)-quinazolinyl]methyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 29 OF 43 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2001:762976 CAPLUS
DOCUMENT NUMBER: 135:303906
TITLE: Preparation of quinazolines useful in the production of an antiangiogenic and/or vascular permeability reducing effect in a warm-blooded animal
INVENTOR(S): Hennequin, Laurent Francois Andre; Stokes, Elaine Sophie Elizabeth
PATENT ASSIGNEE(S): Astrazeneca AB, Swed.; Astrazeneca UK Limited
SOURCE: PCT Int. Appl., 103 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2001077085 | A1 | 20011018 | WO 2001-GB1514 | 20010403 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2403365 | AA | 20011018 | CA 2001-2403365 | 20010403 |
| BR 2001009828 | A | 20021217 | BR 2001-9828 | 20010403 |
| EP 1274692 | A1 | 20030115 | EP 2001-921530 | 20010403 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | | |
| JP 2003530387 | T2 | 20031014 | JP 2001-575560 | 20010403 |
| NZ 521421 | A | 20040924 | NZ 2001-521421 | 20010403 |
| AU 779695 | B2 | 20050210 | AU 2001-48507 | 20010403 |
| ZA 2002007382 | A | 20031215 | ZA 2002-7382 | 20020913 |
| NO 2002004763 | A | 20021119 | NO 2002-4763 | 20021003 |
| US 2003191308 | A1 | 20031009 | US 2002-240658 | 20021003 |
| PRIORITY APPLN. INFO.: | | | EP 2000-400967 A | 20000407 |
| | | | EP 2000-400968 A | 20000407 |
| | | | EP 2000-401033 A | 20000413 |
| | | | EP 2000-401034 A | 20000413 |
| | | | WO 2001-GB1514 W | 20010403 |

OTHER SOURCE(S): MARPAT 135:303906
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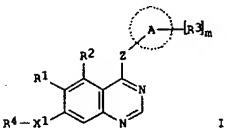
L4 ANSWER 29 OF 43 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



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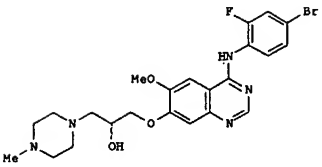


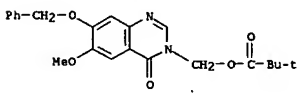
II

AB The title compds. [I; ring A = Ph, 5-6 membered heterocyclic ring; Z = O, NH, S; m = 0-5; R1 = H, OH, halo, etc.; R2 = H, OH, halo, etc.; R3 = OH, halo, alkyl, etc.; provided that when ring A = 5-6 membered heterocyclic ring, at least one R3 is either OH or halo; X1 = O, CH2, S, etc.; R4 = is selected from a number of groups defined herein comprising an alkylene, alkenylene or alkynylene chain wherein each methylene group (other than that of the α-carbon) is optionally substituted by 1 substituent independently selected from OH, halo, NH2 and alkanoyloxy], useful in disease states such as cancer, rheumatoid arthritis and psoriasis, were prepared and formulated. E.g., a multi-step synthesis of the quinazoline II which showed IC50 of 0.015-0.05 μM against the tyrosine kinase activity associated with VEGF receptor (KDR; in vitro), was given.

IT **193002-24-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of quinazolines useful in the production of an antiangiogenic and/or vascular permeability reducing effect in a warm-blooded animal)

RN 193002-24-3 CAPLUS

CN Propanoic acid, 2,2-dimethyl-, [6-methoxy-4-oxo-7-(phenylmethoxy)-3(4H)-quinazolinyl]methyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS

L4 ANSWER 29 OF 43 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 30 OF 43 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:676589 CAPLUS
DOCUMENT NUMBER: 135:227013
TITLE: Preparation of quinazolinylureas and analogs as VEGF receptor antagonists
INVENTOR(S): Hennequin, Laurent Francois Andre; Crawley, Graham Charles; McKerrecher, Darren; Ple, Patrick; Poyser, Jeffrey Philip; Lambert, Christine Marie Paul
PATENT ASSIGNEE(S): Astrazeneca AB, Swed.; Astrazeneca UK Limited
SOURCE: PCT Int. Appl., 170 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2001066099 | A2 | 20010913 | WO 2001-GB863 | 20010301 |
| WO 2001066099 | A3 | 20020321 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| EP 1272185 | A2 | 20030108 | EP 2001-907938 | 20010301 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | | |
| JP 2003525897 | T2 | 20030902 | JP 2001-564752 | 20010301 |
| US 2003225111 | A1 | 20031204 | US 2002-220140 | 20020828 |
| PRIORITY APPLN. INFO.: | | | EP 2000-400595 A | 20000306 |
| | | | WO 2001-GB863 W | 20010301 |

OTHER SOURCE(S): MARPAT 135:227013
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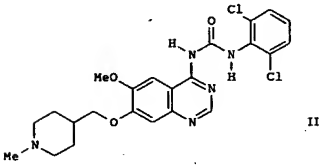
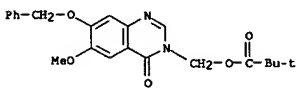

II

AB Q1NR2C(:X)NR3Q2 [I; Q1 = e.g., (un)substituted 4-quinazolinyl; Q2 =

L4 ANSWER 30 OF 43 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
(un)substituted (hetero)aryl(alkyl), cycloalkyl, etc.; R2,R3 = H or alkyl; R2R3 = (CH2)1-3; X = O, S, NCN, (alkyl)imino] were prepd. Thus, Et piperidine-4-carboxylate was converted in 7 steps to Et 2-amino-5-methoxy-4-(1-methylpiperidine-4-ylmethoxy)benzoate which was cyclocondensed with HC(:NH)NH2.HOAc and the product converted in 4 steps to title compd. II. Data for biol. activity of I were given.

IT 193002-24-3P, 7-Benzyloxy-6-methoxy-3-pivaloyloxymethyl-3,4-dihydroquinazolin-4-one
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of quinazolinylureas and analogs as VEGF receptor antagonists)

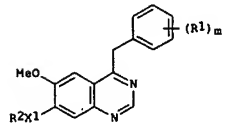
RN 193002-24-3 CAPLUS
CN Propanoic acid, 2,2-dimethyl-, [6-methoxy-4-oxo-7-(phenylmethoxy)-3(4H)-quinazolinyl]methyl ester (9CI) (CA INDEX NAME)



L4 ANSWER 31 OF 43 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:338522 CAPLUS
DOCUMENT NUMBER: 134:353317
TITLE: Preparation of 4-anilino-7-piperidinyloxyquinazolines as vascular endothelial growth factor inhibitors.
INVENTOR(S): Hennequin, Laurent Francois Andre; Stokes, Elaine Sophie Elizabeth; Thomas, Andrew Peter
PATENT ASSIGNEE(S): Astrazeneca AB, Swed.; Astrazeneca UK Ltd.
SOURCE: PCT Int. Appl., 61 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2001032651 | A1 | 20010510 | WO 2000-GB4181 | 20001101 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2389767 | AA | 20010510 | CA 2000-2389767 | 20001101 |
| BR 2000015203 | A | 20020716 | BR 2000-15203 | 20001101 |
| EP 1244647 | A1 | 20021002 | EP 2000-974667 | 20001101 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | | |
| JP 2003513089 | T2 | 20030408 | JP 2001-534802 | 20001101 |
| JP 3522727 | B2 | 20040426 | | |
| EE 200200237 | A | 20030616 | EE 2002-237 | 20001101 |
| AU 769222 | B2 | 20040122 | AU 2001-12886 | 20001101 |
| NZ 518028 | A | 20040326 | NZ 2000-518028 | 20001101 |
| ZA 2002002775 | A | 20031203 | ZA 2002-2775 | 20020409 |
| BG 106659 | A | 20030331 | BG 2002-106659 | 20020426 |
| NO 2002002139 | A | 20020503 | NO 2002-2139 | 20020503 |
| PRIORITY APPLN. INFO.: | | | EP 1999-402759 A | 19991105 |
| | | | EP 1999-402877 A | 19991119 |
| | | | WO 2000-GB4181 W | 20001101 |

OTHER SOURCE(S): MARPAT 134:353317
GI


I

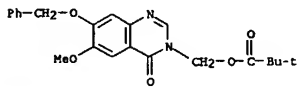
L4 ANSWER 31 OF 43 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

AB Title compds. [I; n = 1-3; R1 = halo, alkyl; X1 = O; R2 = (substituted) piperidin-4-ylalkyl, -alkenyl, -alkynyl], were prepared Thus, 4-chloro-6-methoxy-7-(1-methylpiperidin-4-ylmethoxy)quinazoline (preparation given) and 4-bromo-2-fluoroaniline were refluxed 1.5 h. in Me2CHOH containing HCl to give 90% 4-(4-bromo-2-fluoroanilino)-6-methoxy-7-(1-methylpiperidin-4-ylmethoxy)quinazoline hydrochloride. The latter inhibited VEGF with IC50 = 0.06 μM.

IT **193002-24-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of 4-anilino-7-piperidinyloxyquinazolines as vascular endothelial growth factor inhibitors)

RN 193002-24-3 CAPLUS

CN Propanoic acid, 2,2-dimethyl-, [6-methoxy-4-oxo-7-(phenylmethoxy)-3(4H)-quinazolinyl]methyl ester (9CI) (CA INDEX NAME)



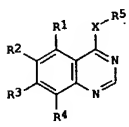
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 32 OF 43 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2001:228867 CAPLUS
DOCUMENT NUMBER: 134:266318
TITLE: Preparation of quinazolines as aurora 2 kinase inhibitors
INVENTOR(S): Mortlock, Andrew Austen; Keen, Nicholas John
PATENT ASSIGNEE(S): Astrazeneca AB, Swed.; Astrazeneca UK Limited
SOURCE: PCT Int. Appl., 208 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2001021597 | A1 | 20010329 | WO 2000-GB3593 | 20000919 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2384296 | AA | 20010329 | CA 2000-2384296 | 20000919 |
| BR 2000014137 | A | 20020521 | BR 2000-14137 | 20000919 |
| TR 200200717 | T2 | 20020621 | TR 2002-200200717 | 20000919 |
| EP 1218355 | A1 | 20020703 | EP 2000-960850 | 20000919 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL | | | | |
| JP 2003509500 | T2 | 20030311 | JP 2001-524976 | 20000919 |
| EE 200200118 | A | 20030415 | EE 2002-118 | 20000919 |
| AU 762697 | B2 | 20030703 | AU 2000-73019 | 20000919 |
| BG 106526 | A | 20021031 | BG 2002-106526 | 20020318 |
| ZA 2002002232 | A | 20030619 | ZA 2002-2232 | 20020319 |
| NO 2002001400 | A | 20020506 | NO 2002-1400 | 20020320 |
| PRIORITY APPLN. INFO.: | | | GB 1999-22171 A | 19990921 |
| | | | WO 2000-GB3593 W | 20000919 |

OTHER SOURCE(S): MARPAT 134:266318
GI



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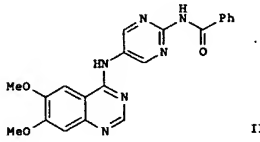


II

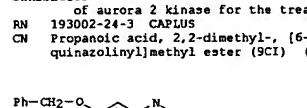
L4 ANSWER 32 OF 43 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

AB Title compds. (I) [wherein X = O, S, SO, SO2, NH, or NR6; R6 = H or alkyl; R5 = (un)substituted 6-membered aromatic ring containing at least one N; R1-R4 = independently halo, CN, NO2, alkylsulfanyl, N(OH)R7, or R9X1; R7 = H or alkyl; X1 = a direct bond, O, CH2, OC(O), CO, S, SO, SO2, or (un)substituted NHCO, CONH, SO2NH, NHSO2, or NH; R9 = H or (un)substituted hydrocarbyl, heterocyclyl, or alkoxy; and at least one of R2 or R3 is other than H; or a salt, ester, amide, or prodrug thereof] were prepared as aurora 2 kinase inhibitors for the treatment of proliferative diseases, such as cancer. For example, 2-(N-benzoylamino)-5-aminopyrimidine and 4-chloro-6,7-dimethoxyquinazoline were coupled in i-PrOH to yield II (58%). The latter inhibited the serine/threonine kinase activity of aurora 2 kinase by 50% at a concentration of 0.00785 μM. In addition, II gave 50% inhibition of MCF-7 cell proliferation at 1.7 μM and reduced BrdU incorporation into cellular DNA by 50% at 1.92-2.848 μM.

IT **193002-24-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediates; preparation of substituted quinazoline derivs. as inhibitors of aurora 2 kinase for the treatment of breast and colorectal cancers)

RN 193002-24-3 CAPLUS

CN Propanoic acid, 2,2-dimethyl-, [6-methoxy-4-oxo-7-(phenylmethoxy)-3(4H)-quinazolinyl]methyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

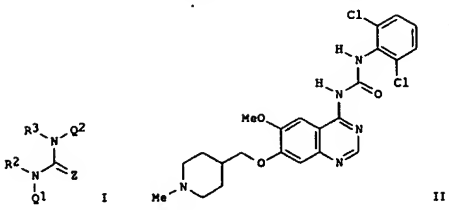
L4 ANSWER 33 OF 43 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2001:50631 CAPLUS
DOCUMENT NUMBER: 134:100885
TITLE: Preparation of quinazolinyl ureas, thioureas and guanidines for use in the prevention or treatment of T cell mediated diseases or medical conditions
INVENTOR(S): Crawley, Graham Charles; McKerrecher, Darren; Poyser, Jeffrey Philip; Hennequin, Laurent Francois Andre; Ple, Patrick; Lambert, Christine Marie-Paul
PATENT ASSIGNEE(S): Astrazeneca UK Limited, UK; Zeneca Pharma S.A.
SOURCE: PCT Int. Appl., 169 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2001004102 | A1 | 20010118 | WO 2000-GB2566 | 20000704 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2378291 | AA | 20010118 | CA 2000-2378291 | 20000704 |
| BR 2000012157 | A | 20020402 | BR 2000-12157 | 20000704 |
| EP 1218353 | A1 | 20020703 | EP 2000-953271 | 20000704 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL | | | | |
| JP 2003504360 | T2 | 20030204 | JP 2001-509712 | 20000704 |
| ZA 2001009864 | A | 20030228 | ZA 2001-9864 | 20011129 |
| NO 2002000042 | A | 20020304 | NO 2002-42 | 20020104 |
| US 6806274 | B1 | 20041019 | US 2002-19945 | 20020107 |
| PRIORITY APPLN. INFO.: | | | EP 1999-401692 A | 19990707 |
| | | | EP 2000-401221 A | 20000504 |
| | | | WO 2000-GB2566 W | 20000704 |

OTHER SOURCE(S): MARPAT 134:100885
GI

L4 ANSWER 33 OF 43 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



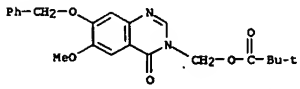
I II

AB The title compds. [I; Q1 = quinazoline ring optionally substituted with halo, CF3 or CN, or a group X1Q3 (wherein X1 = a direct bond, O; Q3 = aryl, arylalkyl, heterocyclyl, (heterocyclyl)alkyl); R2, R3 = H, alkyl; Z = O, S, NH; Q2 = aryl, arylalkyl] and their pharmaceutically-acceptable salts, useful in the prevention or treatment of T cell mediated diseases or medical conditions such as transplant rejection or rheumatoid arthritis, were prepared and formulated. E.g., a multi-step synthesis of the urea II was given. In general, activity possessed by compds. I may be demonstrated at IC50 of 0.0001- 5 μM against enzyme p56lck binding and IC50 of 0.001-10 μM in in vitro T cell proliferation assay (T cell receptor stimulation).

IT **193002-24-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of quinazolinyl ureas, thioureas and guanidines for use in the prevention or treatment of T cell mediated diseases or medical conditions)

RN 193002-24-3 CAPLUS

CN Propanoic acid, 2,2-dimethyl-, [6-methoxy-4-oxo-7-(phenylmethoxy)-3(4H)-quinazolinyl]methyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

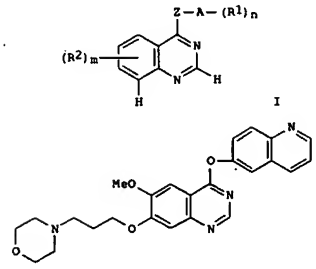
L4 ANSWER 34 OF 43 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2000:573671 CAPLUS
DOCUMENT NUMBER: 133:177183
TITLE: Preparation of quinazoline derivatives as angiogenesis inhibitors
INVENTOR(S): Hennequin, Laurent Francois Andre; Ple, Patrick; Stokes, Elaine Sophie Elizabeth; Mckerrecher, Darren
PATENT ASSIGNEE(S): Astrazeneca UK Limited, UK; Zeneca-Pharma S.A.
SOURCE: PCT Int. Appl., 346 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2000047212 | A1 | 20000817 | WO 2000-GB373 | 20000208 |
| W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2362715 | AA | 20000817 | CA 2000-2362715 | 20000208 |
| EP 1154774 | A1 | 20011121 | EP 2000-902730 | 20000208 |
| EP 1154774 | B1 | 20050622 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | |
| TR 200102314 | T2 | 20020121 | TR 2001-200102314 | 20000208 |
| BR 2000008128 | A | 20020213 | BR 2000-8128 | 20000208 |
| JP 2002536414 | T2 | 20021029 | JP 2000-598164 | 20000208 |
| EE 200100409 | A | 20021216 | EE 2001-409 | 20000208 |
| AU 763618 | B2 | 20030731 | AU 2000-24475 | 20000208 |
| NZ 513204 | A | 20040430 | NZ 2000-513204 | 20000208 |
| ZA 2001006340 | A | 20021101 | ZA 2001-6340 | 20010801 |
| NO 2001003882 | A | 20011009 | NO 2001-3882 | 20010809 |
| PRIORITY APPLN. INFO.: | | | EP 1999-400305 A | 19990210 |
| | | | WO 2000-GB373 W | 20000208 |

OTHER SOURCE(S): MARPAT 133:177183
GI

L4 ANSWER 34 OF 43 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



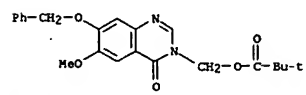
I II

AB The title compds. (I) [wherein A = an 8-, 9-, 10-, 12- or 13-membered bicyclic or tricyclic ring optionally containing 1-3 O, N, and/or S heteroatoms; Z = O, NH, S, CH2, or a bond; n = 0-5; m = 0-3; R2 = H, OH, halo, CN, NO2, CF3, alkyl(sulfanyl), alkoxy, NR3N4, or R5X1; R3 and R4 = independently H or alkyl; X1 = a bond, O, CH2, OC(O), CO, S, SO, SO2, NR6CO, CONR7, SO2R8, NR9SO2, or NR10; R5 = H or (un)substituted alkyl, alkenyl, alkynyl, or heterocyclyl, etc.; R6-R10 = independently H or (alkoxy)alkyl] were prepared for use in the production of an antiangiogenic and/or vascular permeability reducing effect in warm-blooded animals. For instance, II was synthesized in a 9-step sequence starting with the cyclization of 2-amino-4-benzyloxy-5-methoxybenzamide using Gold's reagent in dioxane to form 7-benzyloxy-6-methoxy-3,4-dihydroquinazolin-4-one (84%). I and the pharmaceutically acceptable salts thereof inhibit the effects of VEGF, a property of value in the treatment of a number of disease states including cancer and rheumatoid arthritis (no data).

IT **193002-24-3P**, 7-Benzyloxy-6-methoxy-3-[(pivaloyloxy)methyl]-3,4-dihydroquinazolin-4-one
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of quinazolines as angiogenesis inhibitors by cyclization of 2-aminobenzamides and subsequent derivatization)

RN 193002-24-3 CAPLUS

CN Propanoic acid, 2,2-dimethyl-, [6-methoxy-4-oxo-7-(phenylmethoxy)-3(4H)-quinazolinyl]methyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

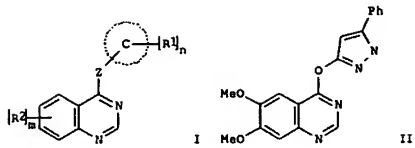
L4 ANSWER 34 OF 43 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

L4 ANSWER 35 OF 43 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:260277 CAPLUS
DOCUMENT NUMBER: 132:293771
TITLE: Preparation of quinazolines as VEGF receptor tyrosine kinase inhibitors
INVENTOR(S): Hennequin, Laurent Francois Andre; Pasquet, Georges
PATENT ASSIGNEE(S): Zeneca Limited, UK; Zeneca-Pharma S.A.
SOURCE: PCT Int. Appl., 107 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2000021955 | A1 | 20000420 | WO 1999-GB3295 | 19991005 |
| W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2344290 | AA | 20000420 | CA 1999-2344290 | 19991005 |
| AU 9961128 | A1 | 20000501 | AU 1999-61128 | 19991005 |
| AU 756556 | B2 | 20030116 | | |
| BR 9914326 | A | 20010626 | BR 1999-14326 | 19991005 |
| EP 1119567 | A1 | 20010801 | EP 1999-947758 | 19991005 |
| EP 1119567 | B1 | 20050504 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | |
| JP 2002527436 | T2 | 20020827 | JP 2000-575861 | 19991005 |
| NZ 510434 | A | 20031031 | NZ 1999-510434 | 19991005 |
| AT 294796 | E | 20050515 | AT 1999-947758 | 19991005 |
| ZA 2001002655 | A | 20020930 | ZA 2001-2655 | 20010330 |
| NO 2001001739 | A | 20010607 | NO 2001-1739 | 20010406 |
| PRIORITY APPLN. INFO.: | | | EP 1998-402496 A | 19981008 |
| | | | WO 1999-GB3295 W | 19991005 |

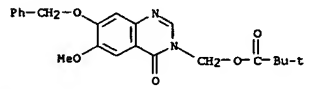
OTHER SOURCE(S): MARPAT 132:293771
GI

L4 ANSWER 35 OF 43 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



I II

AB The title compds. [I; ring C = 5-6 membered heterocyclic moiety; Z = O, NH, S, CH2; R1 = H, alkyl, alkoxymethyl, etc.; n = 0-5; m = 0-3; R2 = H, OH, halo, etc.] and their salts which inhibit the effects of VEGF , and therefore useful in the production of an antiangiogenic and/or vascular permeability reducing effect in warm-blooded animals, were prepared and formulated. E.g., a multi-step synthesis of quinazoline II was given. Compds. I are effective at 1-50 mg/kg/day.
IT 193002-24-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of quinazolines as VEGF receptor tyrosine kinase inhibitors)
RN 193002-24-3 CAPLUS
CN Propanoic acid, 2,2-dimethyl-, [6-methoxy-4-oxo-7-(phenylmethoxy)-3(4H)-quinazolinyl]methyl ester (9CI) (CA INDEX NAME)



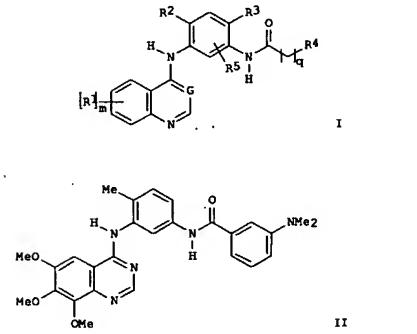
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 36 OF 43 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:241203 CAPLUS
DOCUMENT NUMBER: 132:265207
TITLE: Preparation of 4-anilinoquinazolines and 4-anilinoquinolines as inhibitors of cytokine mediated disease
INVENTOR(S): Cumming, John Graham
PATENT ASSIGNEE(S): Zeneca Limited, UK
SOURCE: PCT Int. Appl., 101 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2000020402 | A1 | 20000413 | WO 1999-GB3220 | 19990927 |
| W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2341374 | AA | 20000413 | CA 1999-2341374 | 19990927 |
| AU 9961064 | A1 | 20000426 | AU 1999-61064 | 19990927 |
| AU 761552 | B2 | 20030605 | | |
| BR 9914162 | A | 20010626 | BR 1999-14162 | 19990927 |
| EP 1117653 | A1 | 20010725 | EP 1999-947686 | 19990927 |
| EP 1117653 | B1 | 20030205 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | |
| JP 2002526538 | T2 | 20020820 | JP 2000-574519 | 19990927 |
| AT 232205 | E | 20030215 | AT 1999-947686 | 19990927 |
| NZ 510210 | A | 20030630 | NZ 1999-510210 | 19990927 |
| PT 1117653 | T | 20030630 | PT 1999-947686 | 19990927 |
| ES 2191462 | T3 | 20030901 | ES 1999-947686 | 19990927 |
| ZA 2001002187 | A | 20020618 | ZA 2001-2187 | 20010315 |
| US 6593333 | B1 | 20030715 | US 2001-787883 | 20010323 |
| NO 2001001631 | A | 20010521 | NO 2001-1631 | 20010330 |
| HK 1037367 | A1 | 20030822 | HK 2001-108138 | 20011119 |
| US 2003216417 | A1 | 20031120 | US 2003-441084 | 20030520 |
| US 6716847 | B2 | 20040406 | | |
| PRIORITY APPLN. INFO.: | | | GB 1998-21338 A | 19981001 |
| | | | GB 1999-6564 A | 19990323 |
| | | | WO 1999-GB3220 W | 19990927 |
| | | | US 2001-787883 A3 | 20010323 |

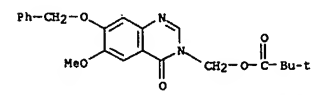
OTHER SOURCE(S): MARPAT 132:265207
GI

L4 ANSWER 36 OF 43 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



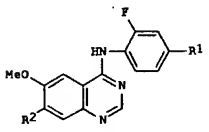
I II

AB The title compds. [I; G = N, CH; R1 = OH, halo, CF3, etc.; R2, R3 = H, halo, alkyl, etc.; R4 = H, OH, alkyl, etc.; R5 = H, halo, CF3; m = 1-3; q = 0-4] and their pharmaceutically acceptable salts or in vivo cleavable esters, useful in the treatment of diseases or medical conditions mediated by cytokines, were prepared and formulated. E.g., a multi-step synthesis of II which showed IC50 of 0.2 μM against p38α kinase and IC50 of 5.2 μM against TNFα production, was given.
IT 193002-24-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of 4-anilinoquinazolines and 4-anilinoquinolines as inhibitors
of cytokine mediated disease)
RN 193002-24-3 CAPLUS
CN Propanoic acid, 2,2-dimethyl-, [6-methoxy-4-oxo-7-(phenylmethoxy)-3(4H)-quinazolinyl]methyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 37 OF 43 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:784580 CAPLUS
DOCUMENT NUMBER: 132:151769
TITLE: Design and Structure-Activity Relationship of a New Class of Potent VEGF Receptor Tyrosine Kinase Inhibitors
AUTHOR(S): Hennequin, Laurent F.; Thomas, Andrew P.; Johnstone, Craig; Stokes, Elaine S. E.; Ple, Patrick A.; Lohmann, Jean-Jacques M.; Ogilvie, Donald J.; Dukes, Mike; Wedge, Steve R.; Curwen, Jon O.; Kendrew, Jane; Lambert-van der Brempt, Christine
CORPORATE SOURCE: AstraZeneca Zeneca Pharma Centre de Recherches Z.I. La Pompelle, Reims, 51689, Fr.
SOURCE: Journal of Medicinal Chemistry (1999), 42(26), 5369-5389
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

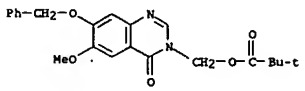


I

AB A series of substituted 4-anilinoquinazolines and related compds. were synthesized as potential inhibitors of vascular endothelial growth factor (VEGF) receptor (Flt and KDR) tyrosine kinase activity. Enzyme screening indicated that a narrow structure-activity relationship (SAR) existed for the bicyclic ring system, with quinazolines, quinolines, and cinnolines having activity and with quinazolines and quinolines generally being preferred. Substitution of the aniline was investigated and clearly indicated that small lipophilic substituents such as halogens or Me were preferred at the C-4' position. Small substituents such as hydrogen and fluorine are preferred at the C-2' position. Introduction of a hydroxyl group at the meta position of the aniline produced the most potent inhibitors of Flt and KDR tyrosine kinases activity with IC50 values in the nanomolar range. Investigation of the quinazoline C-6 and C-7 positions indicates that a large range of substituents are tolerated at C-7, whereas variation at the C-6 is more restricted. At C-7, neutral, basic, and heteroarom. side chains led to very potent compds., as illustrated by the methoxyethoxy derivative I [R1 = 4-Cl, R2 = OCH2CH2OMe] (IC50 < 2 nM). These inhibitors proved to be very selective inhibitors of Flt and KDR tyrosine kinase activity when compared to that associated with the FGF receptor (50- to 3800-fold). Observed enzyme profiles translated well with respect to potency and selectivity for inhibition of growth factor stimulated proliferation of human umbilical vein endothelial cells (HUVECs). Oral administration of selected compds. to mice produced total plasma levels 6 h after dosing of between 3 and 49 μM. In vivo efficacy was demonstrated in a rat uterine edema assay where significant activity was achieved at 60 mg/kg with I [R1 = Me, R2 = OMe]. Inhibition of growth of human tumors in athymic mice has also been demonstrated: I [R1 = Br, R2 = 2-(1,2,3-triazol-1-yl)ethoxy] inhibited the growth of established Calu-6 lung carcinoma xenograft by 75% (P < 0.001, one tailed t-test) following daily oral administration of 100 mg/kg for 21 days.

IT 193002-24-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and structure-activity relationship of arylaminoquinazoline VEGF receptor tyrosine kinase inhibitors)

RN 193002-24-3 CAPLUS
CN Propanoic acid, 2,2-dimethyl-, [6-methoxy-4-oxo-7-(phenylmethoxy)-3(4H)-quinazolinyl]methyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 79 THERE ARE 79 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 38 OF 43 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:166618 CAPLUS
DOCUMENT NUMBER: 130:209715
TITLE: Preparation of oxindolylquinazolines as angiogenesis inhibitors
INVENTOR(S): Hennequin, Laurent Francois Andre; Ple, Patrick; Lohmann, Jean-Jacques Marcel; Thomas, Andrew Peter
PATENT ASSIGNEE(S): Zeneca Limited, UK; Zeneca-Pharma S.A.
SOURCE: PCT Int. Appl., 135 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9910349 | A1 | 19990304 | WO 1998-GB2493 | 19980819 |
| W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| AU 9888162 | A1 | 19990316 | AU 1998-88162 | 19980819 |
| EP 1005470 | A1 | 20000607 | EP 1998-939756 | 19980819 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI | | | | |
| JP 2001514182 | T2 | 20010911 | JP 2000-507677 | 19980819 |
| US 6294532 | B1 | 20010925 | US 2000-486051 | 20000503 |

PRIORITY APPLN. INFO.:

| | | |
|---|---|---|
| EP 1997-401972 | A | 19970822 |
| EP 1997-401973 | A | 19970822 |
| EP 1997-401974 | A | 19970822 |
| WO 1998-GB2493 | W | 19980819 |

OTHER SOURCE(S): MARPAT 130:209715
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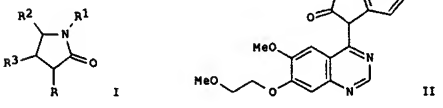


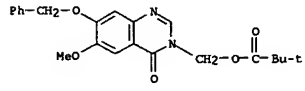
I II

AB Title compds. [I; R = 5-8 (un)substituted 4-quinazolinyl; R1 = H, alkyl, (di)alkoxymethyl, alkanoyl; R2R3 = atoms to complete a heterocyclic ring] were prepared as angiogenesis inhibitors (no data). Thus, 4-chloro-6-methoxy-7-(2-methoxyethoxy)quinazoline (preparation given) was condensed with 7-azaoxindole to give title compound II.

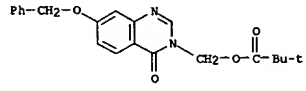
IT 193002-24-3P 196603-88-0P

L4 ANSWER 38 OF 43 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of oxindolylquinazolines as angiogenesis inhibitors)

RN 193002-24-3 CAPLUS
CN Propanoic acid, 2,2-dimethyl-, [6-methoxy-4-oxo-7-(phenylmethoxy)-3(4H)-quinazolinyl]methyl ester (9CI) (CA INDEX NAME)



RN 196603-88-0 CAPLUS
CN Propanoic acid, 2,2-dimethyl-, [4-oxo-7-(phenylmethoxy)-3(4H)-quinazolinyl]methyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 39 OF 43 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:756964 CAPLUS
DOCUMENT NUMBER: 128:22920
TITLE: Oxindolylquinazoline derivatives as angiogenesis inhibitors
INVENTOR(S): Thomas, Andrew Peter; Hennequin, Laurent Francois Andre; Lohmann, Jean-jacques Marcel; Ple, Patrick
PATENT ASSIGNEE(S): Zeneca Limited, UK; Zeneca Pharma S.A.; Thomas, Andrew Peter; Hennequin, Laurent Francois Andre; Lohmann, Jean-Jacques Marcel; Ple, Patrick
SOURCE: PCT Int. Appl., 164 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9742187 | A1 | 19971113 | WO 1997-GB1211 | 19970502 |
| W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
| AU 9726475 | A1 | 19971126 | AU 1997-26475 | 19970502 |
| EP 912557 | A1 | 19990506 | EP 1997-918293 | 19970502 |
| EP 912557 | B1 | 20030709 | | |
| R: CH, DE, FR, GB, IT, LI | | | | |
| JP 2000510115 | T2 | 20000808 | JP 1997-539644 | 19970502 |
| ZA 9703844 | A | 19971106 | ZA 1997-3844 | 19970505 |
| US 6265411 | B1 | 20010724 | US 1998-180310 | 19981106 |
| PRIORITY APPLN. INFO.: | | | EP 1996-400956 A | 19960506 |
| | | | EP 1996-400957 A | 19960506 |
| | | | EP 1996-402762 A | 19961217 |
| | | | EP 1996-402763 A | 19961217 |
| | | | WO 1997-GB1211 W | 19970502 |

OTHER SOURCE(S): MARPAT 128:22920
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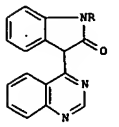

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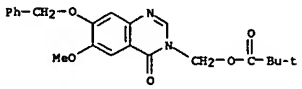
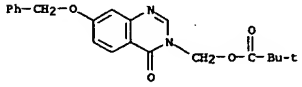
L4 ANSWER 39 OF 43 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

AB Title compds. I [R = H, alkyl, alkoxymethyl, dialkoxymethyl, alkanoyl and the benzene rings may be further substituted] were prepared for use in inhibiting angiogenesis and reducing vascular permeability (no data). Thus, 4,5-dimethoxyanthranilic acid was converted to 6,7-dimethoxyquinazoline by treatment with HCONH2 and was treated with 1-methyloxindole to give 6,7-dimethoxy-4-(1-methyl-3-oxindolyl)quinazoline.
IT 193002-24-3P 196603-88-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of oxindolylquinazoline derivs. as angiogenesis and vascular permeability inhibitors)
RN 193002-24-3 CAPLUS
CN Propanoic acid, 2,2-dimethyl-, [6-methoxy-4-oxo-7-(phenylmethoxy)-3(4H)-quinazolinyl]methyl ester (9CI) (CA INDEX NAME)



RN 196603-88-0 CAPLUS
CN Propanoic acid, 2,2-dimethyl-, [4-oxo-7-(phenylmethoxy)-3(4H)-quinazolinyl]methyl ester (9CI) (CA INDEX NAME)

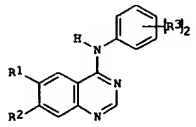


L4 ANSWER 40 OF 43 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:640511 CAPLUS
DOCUMENT NUMBER: 127:278209
TITLE: Preparation of 4-anilinoquinazolines for use in the treatment of disease states associated with antiangiogenesis and/or increased vascular permeability
INVENTOR(S): Thomas, Andrew Peter; Hennequin, Laurent Francois Andre; Johnstone, Craig
PATENT ASSIGNEE(S): Zeneca Ltd., UK; Zeneca Pharma S.A.; Thomas, Andrew Peter; Hennequin, Laurent Francois Andre; Johnstone, Craig
SOURCE: PCT Int. Appl., 72 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9732856 | A1 | 19970912 | WO 1997-GB550 | 19970228 |
| W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
| ZA 9701747 | A | 19980827 | ZA 1997-1747 | 19970227 |
| CA 2244897 | AA | 19970912 | CA 1997-2244897 | 19970228 |
| AU 9718664 | A1 | 19970922 | AU 1997-18664 | 19970228 |
| AU 719327 | B2 | 20000504 | | |
| EP 885198 | A1 | 19981223 | EP 1997-906814 | 19970228 |
| EP 885198 | B1 | 20011219 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI | | | | |
| CN 1212684 | A | 19990331 | CN 1997-192807 | 19970228 |
| CN 1116286 | B | 20030730 | | |
| NZ 331191 | A | 20000327 | NZ 1997-331191 | 19970228 |
| JP 2000517291 | T2 | 20001226 | JP 1997-531552 | 19970228 |
| AT 211134 | E | 20020115 | AT 1997-906814 | 19970228 |
| PT 885198 | T | 20020628 | PT 1997-906814 | 19970228 |
| ES 2169355 | T3 | 20020701 | ES 1997-906814 | 19970228 |
| IL 125954 | A1 | 20030624 | IL 1997-125954 | 19970228 |
| TW 542826 | B | 20030721 | TW 1997-86102593 | 19970304 |
| NO 9804085 | A | 19980904 | NO 1998-4085 | 19980904 |
| NO 311427 | B1 | 20011126 | | |
| US 6291455 | B1 | 20010918 | US 1998-142339 | 19980908 |
| PRIORITY APPLN. INFO.: | | | EP 1996-400468 A | 19960305 |
| | | | EP 1996-401499 A | 19960708 |
| | | | WO 1997-GB550 W | 19970228 |

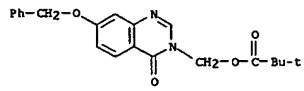
OTHER SOURCE(S): MARPAT 127:278209
GI

L4 ANSWER 40 OF 43 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



I

AB The title compds. [I; R1 = H, MeO; R2 = MeO, EtO, 2-MeO(CH2)2O, etc.; R3 = halo, OH, CN, etc.] and their salts, inhibiting the effects of VEGF, a property of value in the treatment of a number of disease states including cancer and rheumatoid arthritis, were prepared and formulated. Thus, reaction of 4-chloro-7-(2-methoxyethoxy)quinazoline.HCl with 4-chloro-2-fluoroaniline in iPrOH afforded 84% I [R1 = H; R2 = 2-MeO(CH2)2O; R3 = 4-Cl, 2-F]. Compds. I are effective at 1-50 mg/kg.
IT 196603-88-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of 4-anilinoquinazolines for use in the treatment of disease states associated with antiangiogenesis and/or increased vascular permeability)
RN 196603-88-0 CAPLUS
CN Propanoic acid, 2,2-dimethyl-, [4-oxo-7-(phenylmethoxy)-3(4H)-quinazolinyl]methyl ester (9CI) (CA INDEX NAME)



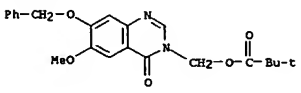
L4 ANSWER 41 OF 43 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1997:502972 CAPLUS
DOCUMENT NUMBER: 127:135808
TITLE: Preparation and antiangiogenic and/or vascular permeability reducing effect of quinazoline derivatives
INVENTOR(S): Lohmann, Jean-Jacques Marcel; Hennequin, Laurent Francois Andre; Thomas, Andrew Peter
PATENT ASSIGNEE(S): Zeneca Limited, UK; Zeneca-Pharma S.A.; Lohmann, Jean-Jacques Marcel; Hennequin, Laurent Francois Andre; Thomas, Andrew Peter
SOURCE: PCT Int. Appl., 162 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9722596 | A1 | 19970626 | WO 1996-GB3075 | 19961213 |
| W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
| CA 2237005 | AA | 19970626 | CA 1996-2237005 | 19961213 |
| AU 9711061 | A1 | 19970714 | AU 1997-11061 | 19961213 |
| AU 712370 | B2 | 19991104 | | |
| EP 873319 | A1 | 19981028 | EP 1996-941787 | 19961213 |
| EP 873319 | B1 | 20010725 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | |
| CN 1205694 | A | 19990120 | CN 1996-199110 | 19961213 |
| CN 1133625 | B | 20040107 | | |
| BR 9612043 | A | 19991228 | BR 1996-12043 | 19961213 |
| JP 2000515114 | T2 | 20001114 | JP 1997-522568 | 19961213 |
| AT 203524 | E | 20010815 | AT 1996-941787 | 19961213 |
| ES 2162656 | T3 | 20020101 | ES 1996-941787 | 19961213 |
| PT 873319 | T | 20020130 | PT 1996-941787 | 19961213 |
| SK 282443 | B6 | 20020205 | SK 1998-828 | 19961213 |
| CZ 291100 | B6 | 20021211 | CZ 1998-1882 | 19961213 |
| RU 2194701 | C2 | 20021220 | RU 1998-113300 | 19961213 |
| ZA 9610597 | A | 19970618 | ZA 1996-10597 | 19961217 |
| US 5962458 | A | 19991005 | US 1996-768887 | 19961217 |
| TW 411274 | B | 20001111 | TW 1996-85115569 | 19961217 |
| NO 9802784 | A | 19980817 | NO 1998-2784 | 19980617 |
| NO 311358 | B1 | 20011119 | | |
| US 6071921 | A | 20000606 | US 1998-203764 | 19981202 |
| US 6258951 | B1 | 20010710 | US 2000-500470 | 20000209 |
| US 2002032208 | A1 | 20020314 | US 2001-877005 | 20010611 |
| US 6362336 | B2 | 20020326 | | |
| GR 3036954 | T3 | 20020131 | GR 2001-401823 | 20011019 |

PRIORITY APPLN. INFO.: EP 1995-402846 A 19951218

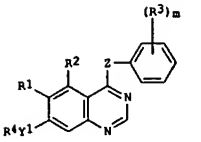
L4 ANSWER 41 OF 43 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



L4 ANSWER 41 OF 43 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

| | | |
|---|---|---|
| | EP 1996-402190 | A 19961015 |
| | EP 1996-941787 | A 19961213 |
| | WO 1996-GB3075 | W 19961213 |
| | US 1996-768887 | A1 19961217 |
| | US 1998-203764 | A1 19981202 |
| | US 2000-500470 | A3 20000209 |

OTHER SOURCE(S): MARPAT 127:135808
GI



I

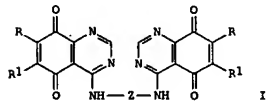
AB Quinazoline derivs. I [Y1 represents -O-, -S-, -CH2-, -SO-, -SO2-, NR5CO-, -CONR6-, -SO2NR7-, -NR8SO2- or -NR9- (wherein R5, R6, R7, R8 and R9 each independently represents hydrogen, alkyl or alkoxyalkyl); R1 represents hydrogen, hydroxy, halo, nitro, trifluoromethyl, cyano, alkyl, alkoxy, alkylthio, amino, alkylamino; R2 represents hydrogen, hydroxy, halo, alkyl, alkoxy, trifluoromethyl, cyano, amino, nitro; m is an integer from 1 to 5; R3 represents hydroxy, halo, alkyl, alkoxy, alkanoyloxy, trifluoromethyl, cyano, amino, nitro; R4 represents a group which is or which contains an optionally substituted pyridone, Ph or aromatic heterocyclic group] were prepared I inhibit the effects of VEGF (no data), a property of value in the treatment of a number of disease states including cancer and rheumatoid arthritis. E.g., heating a mixture of 2-amino-4-benzyloxy-5-methoxybenzamide and Gold's reagent, followed by NaOAc and HOAc, gave 7-benzyloxy-6-methoxy-3,4-dihydroquinazolin-4-one. The product was treated with thionyl chloride, then 3-acetoxy-4-methylaniline, and next hydrogenolyzed to give 4-(3-acetoxy-4-methylanilino)-7-hydroxy-6-methoxyquinazoline hydrochloride. The last was reacted with 4-(bromomethyl)pyridine hydrobromide and treated with aqueous NaOH to give 4-(3-hydroxy-4-methylanilino)-6-methoxy-7-(4-pyridylmethoxy)quinazoline hydrochloride.

IT 193002-24-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and antiangiogenic and/or vascular permeability reducing effect of quinazoline derivs.)

RN 193002-24-3 CAPLUS
CN Propanoic acid, 2,2-dimethyl-, [6-methoxy-4-oxo-7-(phenylmethoxy)-3(4H)-quinazolinyl]methyl ester (9CI) (CA INDEX NAME)

L4 ANSWER 42 OF 43 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1989:212749 CAPLUS
DOCUMENT NUMBER: 110:212749
TITLE: Heterocyclic quinones. XIII. Dimerization in the series of 5,8-quinazolinediones: synthesis and antitumor effects of bis(4-amino-5,8-quinazolinediones)
AUTHOR(S): Giorgi-Renault, Sylviane; Renault, Jean; Baron, Michel; Gebel-Servolles, Patricia; Delic, Jozo; Cros, Suzanne; Paoletti, Claude
CORPORATE SOURCE: Fac. Sci. Pharm. Biol., Univ. Rene Descartes, Paris, 75270, Fr.
SOURCE: Chemical & Pharmaceutical Bulletin (1988), 36(10), 3933-47
CODEN: CPBTAL; ISSN: 0009-2363
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 110:212749
GI



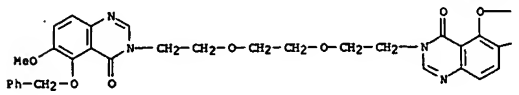
I

AB A series of dimers, e.g., I [R = H, R1 = OMe; R = R1 = 1-aziridinyl; Z = CH2CH2, (CH2)7, (CH2)3NMe(CH2)3, CH2(CH2OCH2)2CH2], of 5,8-quinazolinediones linked in the 4-position by a simple or a substituted α,ω-diaminopolymethylene chain was studied. The structure-activity relationships of I are discussed as functions of the chain length, presence or absence of other functional groups, nature of these groups, position of the chain, and nature of R and R1. I (R = OMe) showed variable cytotoxicity toward L1210 leukemia cells. I (R = R1 = 1-aziridinyl) which exhibited high cytotoxic activity (IC50 = 0.0037 to 0.018 μM) were further screened in vivo for activity against murine P388 leukemia. The most potent compound was I [R = R1 = 1-aziridinyl; Z = (CH2)3NMe(CH2)3].

IT 120622-47-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and debenzylation of)

RN 120622-47-1 CAPLUS
CN 4(3H)-Quinazolinone, 3,3'-[1,2-ethanediylbis(oxy-2,1-ethanediyl)]bis[6-methoxy-5-(phenylmethoxy)- (9CI) (CA INDEX NAME)

PAGE 1-A



L4 ANSWER 42 OF 43 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

PAGE 1-B

—CH2—Ph

—OMe

L4 ANSWER 43 OF 43 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1968:78244 CAPLUS
DOCUMENT NUMBER: 68:78244
TITLE: Synthesis of 6,7-dihydroxy-2-methyl-4-quinazolone
AUTHOR(S): Gadekar, Shreekrishna M.; Kotsen, Anna M.
CORPORATE SOURCE: Lederle Lab. Div., Amer. Cyanamide Co., Pearl River, NY, USA
SOURCE: Journal of Heterocyclic Chemistry (1968), 5(1), 129-31
CODEN: JHTCAD; ISSN: 0022-152X
DOCUMENT TYPE: Journal
LANGUAGE: English

GI For diagram(s), see printed CA Issue.

AB 3,4-(PhCH2O)2-C6H3CHO reacted with HNO3 to give 2,4,5-(O2N)(PhCH2O)2-C6H2CHO, which upon KMnO4 treatment gave 2,4,5-(O2N)-(PhCH2O)2C6H2CO2H. The latter compound treated with FeSO4 in NH3 gave 2,4,5-(H2N)(PhCH2O)2C6H2CO2H, which upon treatment with Ac2O gave 6,7-dibenzyloxy-2-methyl-4H-3,1-benzoxazin-4-one (I). I treated with NH3 gave 6,7-dibenzyloxy-2-methyl-3H-quinazolin-4-one which upon reduction gave the title compound (II). II was prepared in a higher yield by treatment of I with PhCH2NH2, followed by stepwise reduction

IT 18100-54-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 18100-54-4 CAPLUS

CN 4(3H)-Quinazolinone, 3-benzyl-6,7-bis(benzyloxy)-2-methyl- (8CI) (CA INDEX NAME)